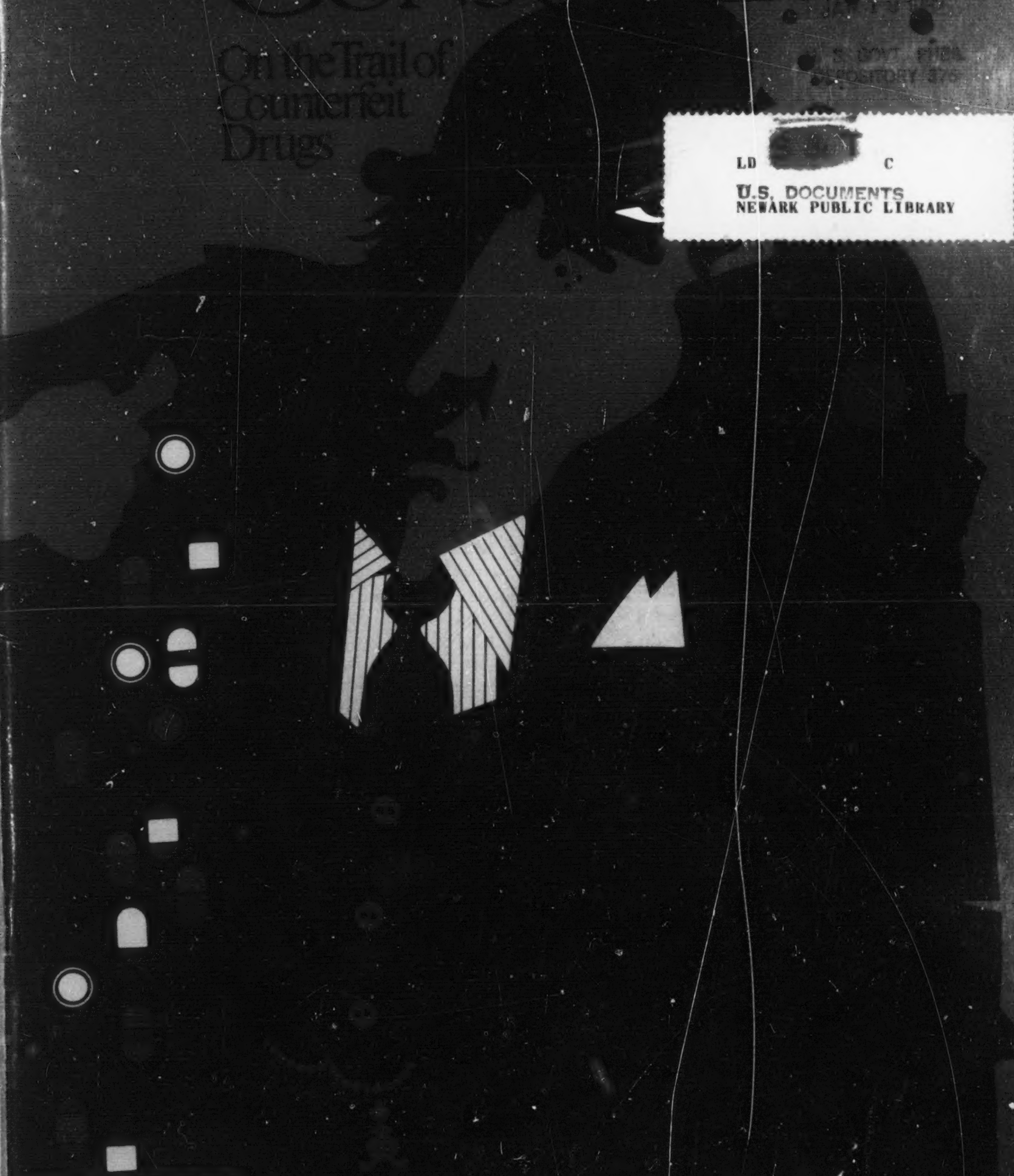
FDA
CONSUMER

December 1981-January 1982

On the Trail of Counterfeit Drugs



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The Truth About Food-Adulteration

By Henry Irving Dodge

Part I. The Microscope Versus Graft

Robb A. Grant

This is the First of a Series of Three Articles, Prepared with the Coöperation of Dr. W. D. Bigelow, Chief of the Division of Foods, United States Bureau of Chemistry. The Series is Therefore a Thoroughly Authoritative Account of This Most Dangerous and Ever-Growing Practice

From the time when man put money into the scales against his brother's life food-adulteration has obtained. Man's weakness was never expressed in form more mean than this. To poison for a patriotic purpose, or even for revenge, has the redeeming quality of romance, but to do it for money degrades the poisoner from the classic dignity of Borgia to the low condition of "Suicide Hall McGuirk."

Perhaps the romance that attaches to poisoning done for murder springs from the passion that prompts the act, the magnificent risk involved, and the picturesque, yet terrible, end of the tragedy. But where the motive is to cheat, the public singularly takes the act none too seriously. By the same token it would bludgeon a highwayman, yet laugh at the escape of a clever pickpocket. It exalts smartness above honesty, and cherishes the bird that feeds upon its vitals, or condones the fact with drowsy toleration. No matter what may be the source of this indifference, the fact is that the public has from a remote period, and does now more broadly than ever, tolerate the adulteration of food for purposes of gain.

Pliny says the Romans put mineral matter into their bread, and doctored their wines to the extent that it was hard to get a glass of the real stuff even in his time. Early Greece saw the danger, and sought to avert it by the appointment of food-inspectors. In the sixteenth century Englishmen tested ale by spilling some on a bench and sitting on it. If their leather breeches stuck to the seat they knew sugar had been added to it. There was nothing complicated about that method. It was not fraught with the arch mystery of chemistry—no blue blazes or sulphurous smoke that bespoke the alchemist. Any boy could practise it, and doubtless many did unconsciously at times. It was a long call from then to 1850, when Hassel replaced the leather-breeches method with analytical chemistry, physics and the microscope, and made disclosures of food-adulteration that startled England into the passage and moderate enforcement of her first national food law.

Thirty years later the seed sown in Great Britain began to sprout in American consciousness. Massachusetts was the first to attempt to enforce food laws, and Minnesota and Ohio soon followed her example. About that time Dr. H. W. Wiley, Chief of the Division (now the Bureau) of Chemistry, began the investigation of foods on the American market. The public was apathetic, bored if you please, by the reiterated efforts of a few patriotic persons, and for more than ten years the movement progressed but slowly, only five states adding their moral support to the stand taken by the other three. In response to an awakened public sentiment, twelve states and territories have within the last six years joined the crusade against poisoned foods. The movement has now become a definite and effective organization. The Association of Official Agricultural Chemists, composed of all federal, state and municipal official chemists, has come into existence. The purpose of this body has been to apply chemical methods to the study of all agricultural products. It has coöperated with Doctor Wiley, Chief of the Bureau of Chemistry, in his work, and has greatly advanced analytical methods for the examination of foods.

Doctor Wiley's efforts presently developed a regular food-examining branch of the Division of Chemistry, which was itself an offshoot of the Department of Agriculture, and when in 1901 it was made a bureau its most important arm was the food laboratory, the affairs of which were administered by Doctor Bigelow, five assistant chemists and a clerk. Three years later, by order of the Secretary of Agriculture, the food laboratory was made the Division of Foods of the Bureau of Chemistry, with a force of sixteen chemists, two clerks and five helpers. The growth of the Division of Foods is typical of that of the Bureau of Chemistry in all fields. From a humble, almost accidental, origin it has grown to be the most important arm of the bureau. In addition to the work of its regular staff the chief of the bureau devotes much detailed personal attention, especially in the establishment of standards of compositions of foods, experiments regarding the influence of preservatives on nutrition, and the enforcement of the foreign food law, which is under his immediate supervision.

A LATE PORTRAIT OF DR. H. W. WILEY CHIEF OF THE UNITED STATES BUREAU OF CHEMISTRY

DR. W. D. BIGELOW, CHIEF OF THE DIVISION OF FOODS, UNITED STATES BUREAU OF CHEMISTRY

Every means known to science has been used by the Bureau of Chemistry to detect food-adulteration. A drag-net, no respecter of persons, was cast for samples. Morse's Four Corners as well as Greater New York contributed to the catch. The corps of the bureau, typical of all other government corps, being drafted from all parts of the country, peculiarly lent itself to the work. When one of the clerks went to his home in San Francisco on a vacation he was accorded a few extra days and expenses and directed to bring back with him samples of foods gathered from all parts of that section. The same with the man from Maine. Thus the whole nation was practically raked, and there was scarcely an article of food which did not contribute to the work of the Bureau of Chemistry. Dairy products, spices and condiments, alcoholic beverages, lard, baking-powder, sugar, confectionery, honey and beeswax, tea, coffee and cocoa preparations, canned vegetables, cereals and cereal products, preserved meat, fruits and fruit products, olive oil, were all subjected to the test.

Doctor Bigelow on one occasion went into the shop of a small importer in New York, and asked for a sample of Rhine wine. "What brand have you?" he asked of the shopkeeper.

"Any brand you desire," said the man; and after some talk he offered to put up a dozen cases of wine for his customer under the label of any one of a number of German wine-makers.

"Can you give me the ——'s liebfraumilch?" asked the Doctor.

The man went to a drawer and got the required label.

"Have you the cap?"

"Yes, sir," said the man, producing it.

Later, going into the store of an alleged importer of wines in Philadelphia, Doctor Bigelow asked an Irish laborer who was temporarily in charge if he could give him a certain make of Rhine wine. The man replied that he did not know where their Rhine wine came from, but that the vineyard was somewhere in California.

A label which the Doctor secured read, "Old reliable coffee"—giving the manufacturer's name—"one pound, full weight. A compound of delicious drinking coffees, guaranteed to please those who like a full, heavy-bodied cup of coffee.

FDA CONSUMER

VOL. 15 NO. 10 **DECEMBER 1981-JANUARY 1982**

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Implanted plastic lenses are being used to replace lenses destroyed by disease or damaged by injury. To date, the operations have been controlled experiments, but official approval is at hand.

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They got their meals free but they had to agree to eat a little poison for the gratuity. That was the poison squad, circa 1906. It was a primitive but effective way of testing food additives.

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They're purple and shaped like lima beans. They are involved in processing nutrients and can influence blood pressure. This article tells just how those kidneys operate.

Drugs Are Dear to Many Hearts 16
Chest pains are treated by a number of drugs. Likewise, the side effects of those drugs can also be treated. What drugs are used and how they work are described in this article.

On the Trail of Counterfeit Drugs 20
From official documents and other sources, the story of look-alike, non-prescription drugs is told. Made to look like recreational "uppers" and "downers," the drugs have proved to be less than benign, leading federal officials to action.

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Food adulteration was a prevalent problem in 1905, as indicated by the reproduced page (left) from the March issue of Woman's Home Companion *magazine. That was the first of three articles on the subject. Such articles helped bring about the passage of the first Food and Drugs Act a year later. Also helping to bring about passage of that law, as well as helping to test for toxic food additives, was the poison squad. The story of that adventuresome group is told in* The Squad That Ate Poison, *starting on page 6.*

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Section 705 [375] of the Food, Drug, and Cosmetic Act:
(a) The Secretary shall cause to be published from time to time reports summarizing all judgments, decrees, and court orders which have been rendered under this Act, including the nature of charge and the disposition thereof.
(b) The Secretary may also cause to be disseminated information regarding food, drugs, devices, or cosmetics in situations involving, in the opinion of the Secretary, imminent danger to health, or gross deception of the consumer. Nothing in this section shall be construed to prohibit the Secretary from collecting, reporting, and illustrating the results of the investigations of the Department.

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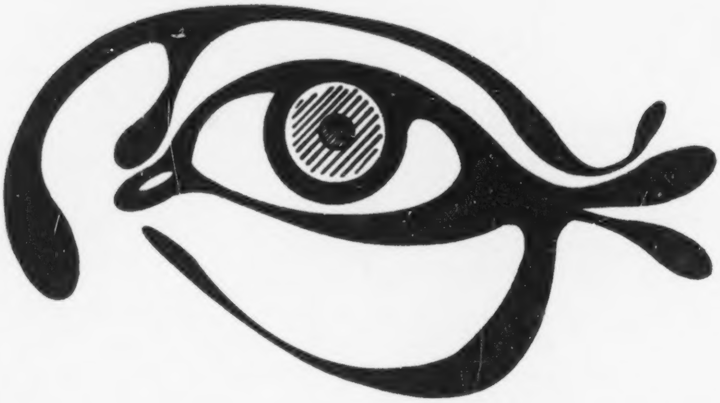
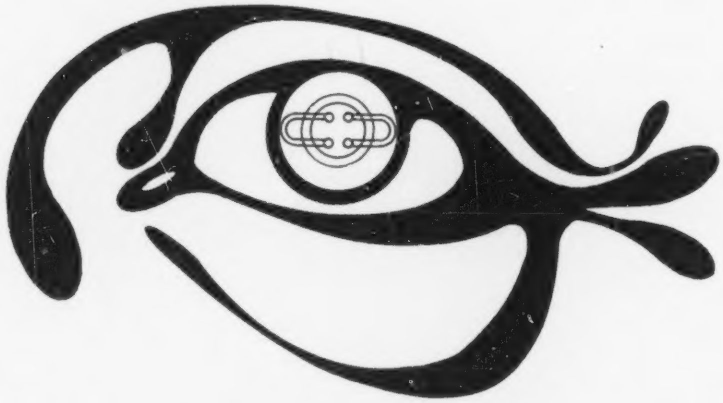




IOLs = New Lenses For Old Eyes

by Donna Lenahan and Bill Rados

When the normally clear lens of the eye becomes clouded by a cataract, vision can be so impaired that the lens must be removed through surgery. The person must then decide what kind of artificial lens to use to bring the world back into focus. Most cataract patients choose eyeglasses; they're inexpensive and easy to handle. But the extra-thick "Coke-bottle" lenses in cataract eyeglasses usually afford poor peripheral vision and unnaturally magnify images to the point where coordinating vision with movement becomes difficult.

Contact lenses partially overcome these difficulties, producing less visual distortion and adequate side vision. But many elderly people—the main victims of cataracts—find the tiny plastic discs hard to handle and uncomfortable to wear.

To avoid the problems of eyeglasses and contact lenses, many cataract patients in recent years have opted for intraocular lenses (IOLs). In many cases these artificial lenses, surgically implanted in the eye close to the normal position of the natural lens, can provide good vision without the hassles of contacts or the distortions of glasses. The catch, however, has been that IOLs were considered experimental—unproven technology with uncertain risks.

Now, cataract patients—and others whose natural lenses have been so damaged that they must be removed—have greater assurance that an IOL implant will be a success. For, after more than three and a half years of clinical studies, FDA has granted its first approval of an IOL, a judgment that the approved lens is safe and effective.

The history of IOLs began well before the start of the FDA-monitored clinical studies in 1978. In World War II, British fighter pilots were sometimes injured when the cockpit covers of their planes were shattered by enemy fire, imbedding fragments of the plastic in their eyes. A Royal Air Force flight surgeon, Dr. Harold Ridley, was surprised to find that the fragments did not cause the usual inflammatory reaction that the body ordinarily employs as a defense mechanism against foreign objects. Dr. Ridley figured that this was due to the inert properties of the plastic. As an ophthalmologist, he saw the medical potential of such properties and in 1949 he surgically implanted the first IOL in the eye of a cataract patient.

The lenses were widely used in Europe for years and began gaining acceptance in the United States in the early 1960s. They were a promising technology, restoring near normal vision to thousands of elderly cataract patients. But they were also a relatively new technology for which no long-term safety and effectiveness data existed. There were reports of some serious complications. In October and November, 1975, FDA learned of 11 cases of severe eye infection in IOL patients. Vision was seriously impaired in all 11 cases and removal of the eye was required in five of the 11.

FDA was given authority to require clinical studies of IOLs under the Medical Device Amendments of 1976. Congress, in response to physicians' expressed fears that the development of IOLs would be severely inhibited, directed FDA to ensure that the lenses would continue to be "reasonably available" to investigators to implant while manufacturers collected safety and effectiveness data. The data would enable FDA to decide whether IOLs should be approved for general marketing.

In November 1977, FDA published a regulation outlining the conditions under which implantation of the lenses could continue. The agency issued manufacturing guidelines to reduce the possibility that defective or bacterially contaminated lenses could be distributed to eye surgeons. Physicians implanting the lenses were required to monitor patients closely after IOL surgery and report any complications periodically to the lens manufacturers. Patients were to be fully informed about the risks and benefits of IOLs before implantation.

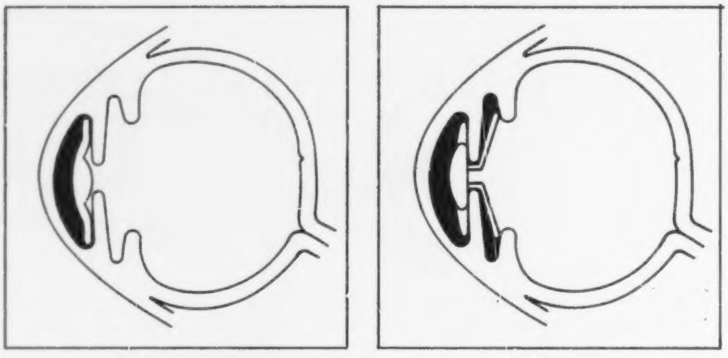
The studies, conducted by 13 manufacturers, began in February 1978. About 70,000 implants were performed the first year; for 1980 the number had grown to 200,000.

Four classes of IOLs have been investigated; their names designate their placement within the eye. Anterior chamber lenses are implanted in front of the iris, the colored part of the eye; posterior chamber IOLs are placed behind the iris. Iris clip and iridocapsular lenses both are implanted even with the iris; they differ in the way they are attached. Each class contains many models and styles.

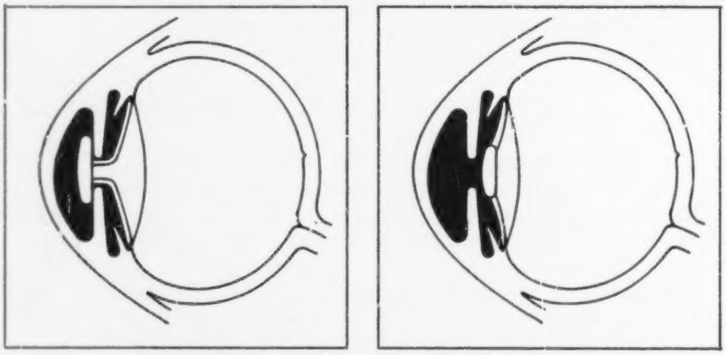
Interim results indicate that the rate of complications from implantation of these lenses is generally not significantly higher than for cataract surgery without an implant. Yet there are differences in the risks. Complications of cataract surgery can include hemorrhage, clouding of the cornea, glaucoma, double vision, swelling, infection and retinal detachment. These problems are also associated with IOL implants as are other complications including irritation or injury of the iris, inability to dilate the pupil, and lens dislocation. These complications may occur weeks, months or even years after the operation and may lead to substantial loss of vision or the need for further surgery.

Between 85 to 90 percent of implant patients in the clinical studies have achieved vision of 20/40 or better. (A person with 20/40 vision can read letters on an eye chart from 20 feet away that a person with normal 20/20 eyesight can read from 40 feet away; 20/40 vision is good enough to get a driver's license in most states.) This level of vision is similar to that achieved with glasses or contact lenses after cataract removal.

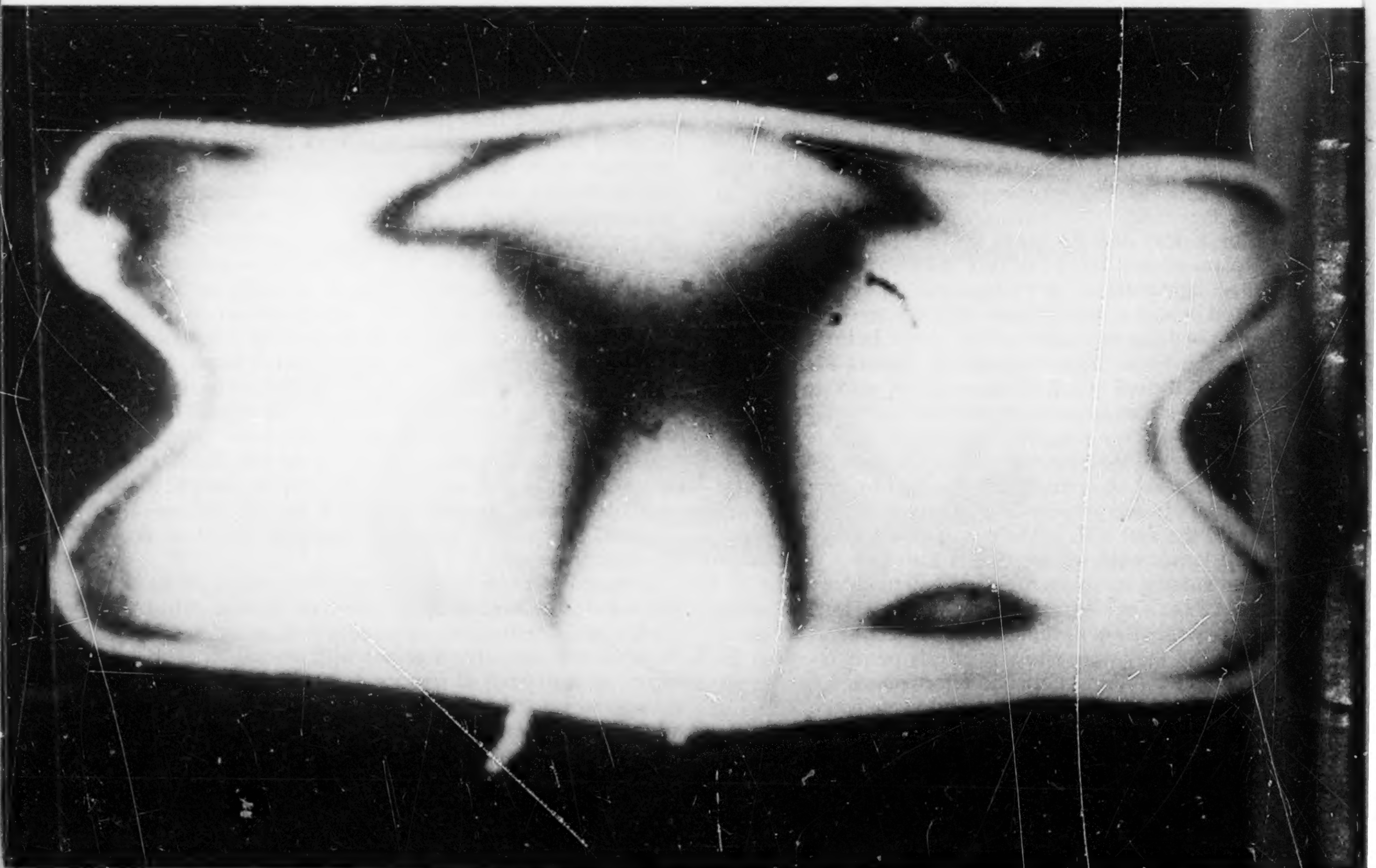
Typical placements of the four classes of intraocular lenses are shown in the drawings at right. Clockwise from upper left is the anterior chamber lens, placed in front of the iris (the colored part of the eye); the iris fixation lens; the posterior chamber lens, implanted behind the iris; and the iridocapsular lens. In the photo below that are stress patterns in an intraocular lens as observed under polarized light. That procedure has been used at the Center for Medical Device Analysis, a part of FDA's Bureau of Medical Devices, to detect possible warping of IOLs.

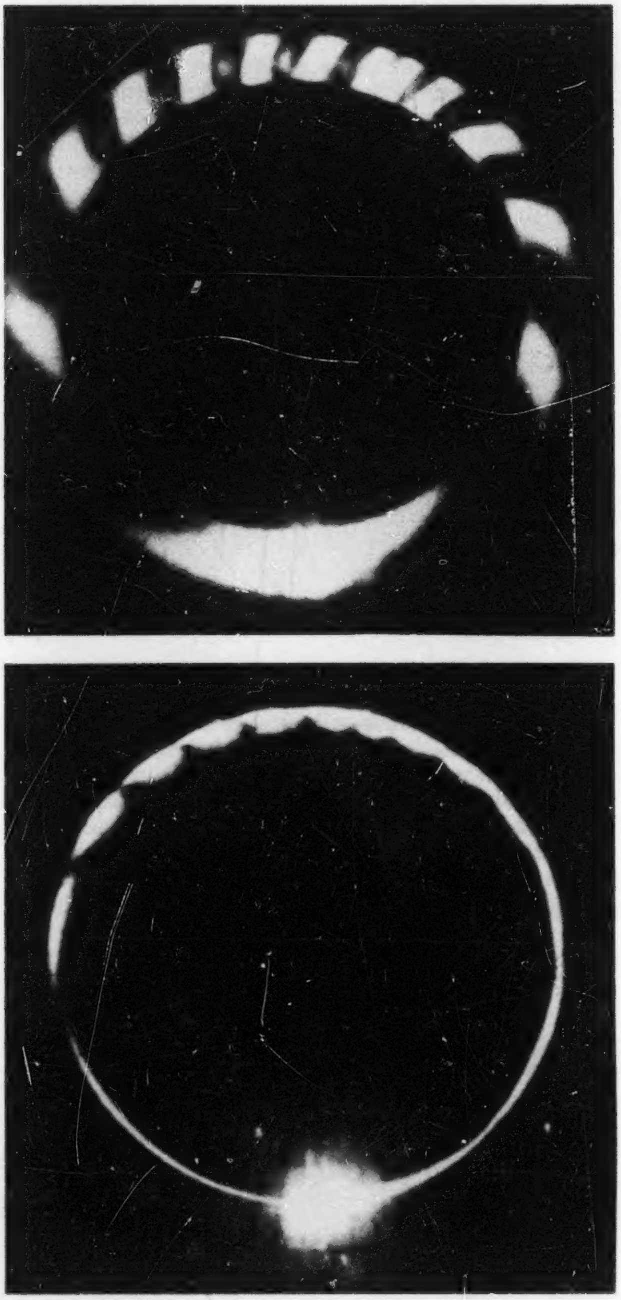


Anterior Chamber **Iris Fixation**



Iridocapsular **Posterior Chamber**





In the photos above, laser beams are used to check the edge of an intraocular lens for any rough spots on it that could injure the eye. The technique was developed at FDA's Center for Medical Device Analysis.

Despite the generally promising results thus far, data from the studies indicate that complication rates and visual acuity do vary with the products of different manufacturers and among different types of lenses.

The studies have not been without controversy. The most vocal critic of the manner in which the investigations have been conducted is Ralph Nader's Health Research Group. The organization called the studies "seriously flawed," but reviews by outside experts, including FDA's Ophthalmic Devices Advisory Section, composed mainly of ophthalmologists and optometrists, concluded that the lenses are being properly studied and the data will be adequate to determine the safety and effectiveness of the lenses.

In fact, FDA has already received applications for premarket approval of 16 types of IOLs, and the first approval was granted last December. Choyce Mark VIII and Choyce Mark IX anterior chamber IOLs from Coburn Optical Systems were determined by FDA to be safe and effective, based on the recommendation of the Ophthalmic Devices Advisory Panel. The panel has reviewed and conditionally recommended approval of other IOLs as well. FDA has told Precision-Cosmet, Inc., IOLab Corp. and Medicornea Division of CooperVision, Inc. that particular styles of their IOLs could be approved soon if certain administrative and labeling requirements are met.

FDA intends to set conditions for its approval of IOLs. The conditions will vary among lens classes and manufacturers, depending on the results of the studies, but generally they will include:

- Establishing a system to help trace lenses from manufacturers to patients and vice versa. Patients will continue to receive an identification card and be registered with the company to help in identifying lenses if problems arise.
- Establishing a toll-free phone number by which physicians can report adverse reactions to the manufacturers; and
- Agreeing to participate in long-term follow-up studies if they are deemed necessary (at present there are no plans for such studies).

Even though various brands and styles of IOLs are likely to receive FDA approval, these lenses will not be suitable for all cataract patients. Patients who have only one eye with potentially good vision and those who have severe glaucoma, diabetic retinopathy, retinal detachment or certain other eye diseases generally are not good candidates for IOLs. Because the clinical studies of IOLs have been largely limited to older patients, the lenses generally should not be used in those under 60. It is not recommended that patients have IOLs implanted in both eyes at the same time.

The patient's decision whether to have an IOL implanted is an individual one that should be made only after discussion with an opthalmologist. Thousands of patients have benefitted greatly from IOLs, but, as with any drug or medical device, success can't be guaranteed. With the physician's advice and guidance, each patient must decide whether the potential benefits of an IOL outweigh the potential risks.

Donna Lenahan is a program analyst in FDA's Bureau of Medical Devices; Bill Rados is on FDA's public affairs staff.

The Squad That Ate Poison

by Wallace F. Janssen

In August 1906, a young chemist with a master's degree arrived in Washington, D.C., from New Hampshire to accept a government job. He was to receive $1,000 a year for laboratory work in the Bureau of Chemistry of the Department of Agriculture. Free board at Dr. Harvey W. Wiley's "hygienic table" was an attractive fringe benefit.

Many young volunteers had been eating the meals prepared in the bureau's kitchen along with carefully measured quantities of commonly used chemical preservatives. The experiments had begun some four years earlier and already much data had been collected.

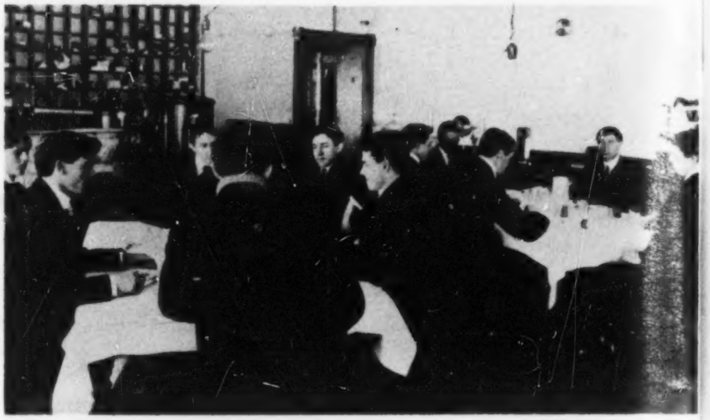
In April 1907, we find our young man seated with seven other volunteers, dining on excellent quality food accompanied by varying quantities of saltpeter, the chemical potassium nitrate. Dr. Wiley, who worked late frequently, joined the group for the evening meal. One such night, Wiley placed his order with Will Carter, waiter at the bureau's boarding house: "Two English mutton chops for me tonight, Will."

Having been served, the "father of the Pure Food Law" (and a noted bon vivant) began to chomp on and swallow his meal with characteristic gusto. Whereupon, the young scientist from New Hampshire brashly spoke up, asking his boss what he thought of "Fletcherism." Horace Fletcher, advocate of prolonged chewing of food as the way to good health and long life, was a popular topic of conversation in 1907.

"The *carnivorae* have bolted meat for years and years, and so shall I," was Wiley's gruff reply.

This story of a meal with Wiley and the "poison squad" was one related by the late William O. Robinson of Falls Church, Va. By all accounts the human guinea pigs suffered no permanent ill effects, although there was no medical follow-up for long-term effects. The experience didn't seem to harm Robinson. He was 94 years old when he died in 1979.

The "poison squad" was not one but several. Enrollment changed considerably over the five years of the project. Among those on the squad with Robinson were Cleon O. Dodge, a classmate at the University of New Hampshire, and also a chemist in the bureau. Another was O. N. Wyatt, a social secretary at the White House and a professional penman, whose duties included the preparation of place cards for state dinners. Still another was Earnest Eaton, an Australian on the embassy staff. Prestige was certainly one of the squad's attractions, along with the free board. Individually anonymous, they were collectively famous from the start.



The poison squad is shown here at lunch in the dining room assigned to the group in the Bureau of Chemistry building. The room also did double duty as part of the road materials laboratory, which probably explains why the pigeonholes in left background contain pieces of rock and other material.

The food of each member of the table under observation was weighed or measured; the liquids, such as coffee, milk, tea and water, were measured and calculated to weight from the density of the solution. Dr. Harvey Wiley displays a torsion balance, sensitive to half a gram, on which solid foods were weighed.

Even at the turn of the century the safety of chemicals used in food was not a new problem. Federal studies of food adulteration, begun in the 1870s, were expanded when Wiley became chief of the Division of Chemistry in 1883. Preservatives used in canned meats and vegetables were the subject of special investigations done for Congress in 1891 and 1893, respectively.

Reporting on the 1893 investigation, Dr. Wiley concluded: "First, [that] the use of added preservatives is, upon the whole, objectionable; second, [that] their absolute inhibition is not warranted by the facts which have come to our knowledge, but in all cases their presence should be marked upon the label. . . ." His views did not change. As to food additives, Wiley was never a total prohibitionist, but remained committed to the need for scientific facts concerning the safety of any substance used in food.

In 1899 the Senate Committee on Manufactures held hearings on food adulteration, Dr. Wiley serving as its scientific expert. Legislation drafted by Wiley and introduced by Senator W. B. Hepburn eventually became the Food and Drugs Act of 1906. In the same year (1899), Wiley recommended that Congress appropriate funds for a major investigation on "whether preservatives should ever be used or not, and if so, what preservatives and in what quantities." He even proposed the language to be inserted in the bill:

> *To enable the Secretary of Agriculture to investigate the character of proposed food preservatives and coloring matters, to determine their relation to digestion and to health, and to establish the principles which should guide their use, for the purchase of the necessary apparatus and supplies, employment of experts and assistants in the conduct of the investigation, and for necessary labor, supplies, traveling expenses in connection therewith, five thousand dollars.*

Three years later, in 1902, Congress approved the project. One reason, no doubt, was that it already had approved legislation to require inspection of imported foods and to reject adulterated shipments. This involved preservatives.

Another reason for congressional support was the considerable variation in food regulations among different countries and the various states. Uniform control was clearly needed.

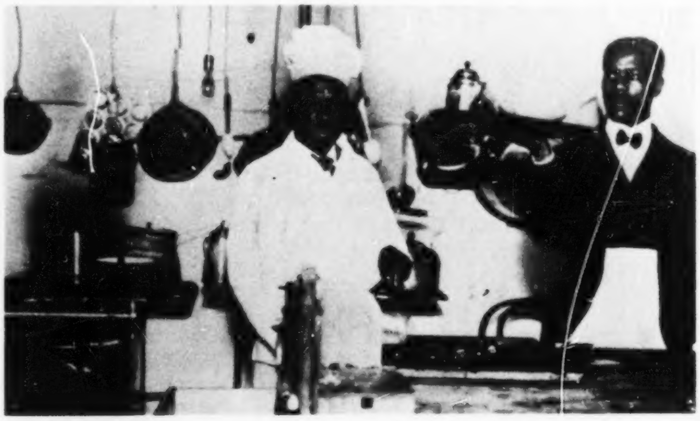
That Wiley had his plans ready is shown by his prompt action in setting up the project. A kitchen and dining room were installed at 1366 B Street S.W., now Independence Avenue. Recruiting of the volunteers began with a statement about the object of the experiments, which Wiley sent to young men in the agriculture department, most of them college graduates or students engaged in scientific programs at low pay. The free meals, Wiley wrote later, were "a very small reward for the restrictions under which they were compelled to live for so long a period. Nevertheless, large numbers of volunteers presented themselves, far in excess of the actual demand."

Those selected signed releases agreeing not to hold the department or any of its employees responsible for any illness or accident connected with the experiments. They pledged to serve at least six months, and were also to continue their daily vocations in the usual way. At the end of a test they were required to certify that they had adhered to all instructions and requirements.

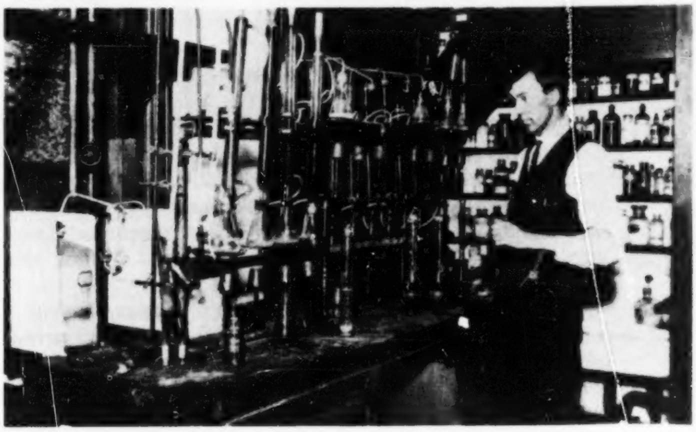
The pledge required of the men was revealing: they promised to eat all of their meals at the "hygienic table" and to consume no other foods or beverages, except water, which was to be measured and reported. They had to fill out a lengthy questionnaire on their dietary habits and health, and to undergo weekly comprehensive medical examinations by doctors from the Marine Hospital and Public Health Service. Had they ever had any serious disease? Did they use alcohol or tobacco? Did they ever have indigestion? What kind of exercise did they take?

Each member had to record his weight, temperature and pulse rate before each meal, and what he ate. Most irksome was to collect all urine and feces in containers provided and deliver it daily for analysis by the chemists. The purpose, of course, was to determine the fate of the chemicals under test—were they retained, excreted, or changed in the body, and to what extent?

Most important was to report any symptoms that might be attributed to the preservatives. This, to Wiley, was the major advantage in using human subjects. Animals cannot describe their feelings.

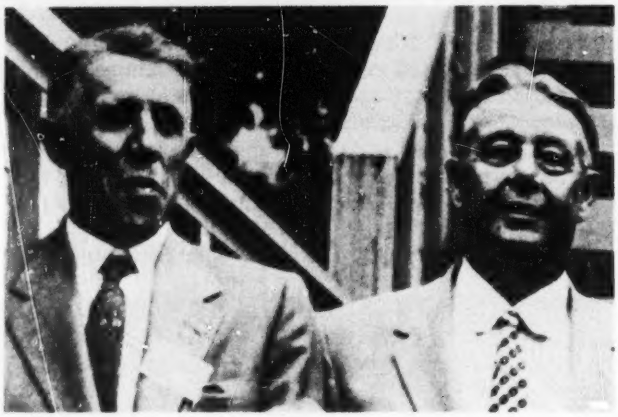


The installation of the kitchen was in one of the rooms in the basement of the Bureau of Chemistry, which up to this time had been used as a storeroom. The cooking was done on two gas stoves and under the supervision of a cook certified by the Civil Service Commission.

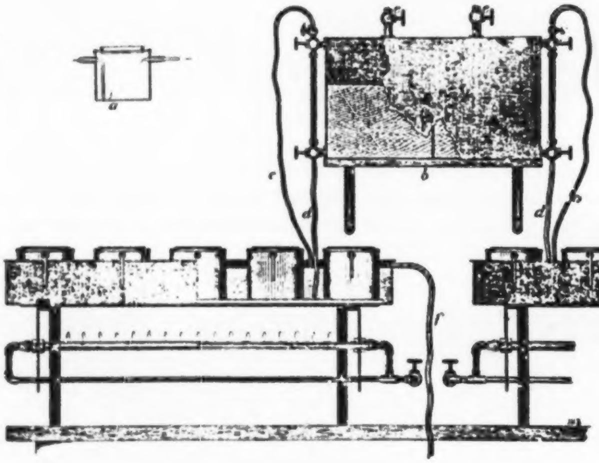


J. T. Keister was one of many Bureau of Chemistry analysts who worked on the poison squad project.

"I have every reason to believe that the members kept their pledges faithfully," wrote Wiley in 1905. "They were young men of fine character and they all took a lively personal interest in the work." Wiley felt this offset the lack of control which would have applied to an animal research population.



Veterans of the poison squad at their 50th class reunion at the University of New Hampshire in 1955: at left, C. O. Dodge; right, William O. Robinson.



Special equipment designed to dry samples of feces for chemical analysis in the poison squad investigations.

The foods were of the highest quality. Generally they were unprocessed, but some canned fruits, vegetables and soups were used. Care was taken to ensure that all cans were from the same batch to assure uniformity and that no preservatives had been added. Coffee and tea were served, but no alcoholic beverages. Moderate and customary use of tobacco was permitted.

Samples of the food as served "were taken for analysis, placed in a bottle, stoppered and sealed with paraffin so that no moisture could escape." All food consumed by each squad member, both solid and liquid, was measured and recorded. "In short," wrote Wiley, "an account was opened with each member of the table, exactly similar to a bank account. Each member was charged with all that was given to him in food and credited with all that was returned in the excretions. The balance represented the food consumed in the production of heat and energy . . . provided the body weight remained constant."

All the studies were similar in design, whatever preservative was being tested. They began with a "fore" period, usually 10 days, in which no chemical was given, to establish the normal state of health of the individual. A particular concern was to determine the amount of food needed to maintain body weight unchanged. Records were kept as to pulse rate, temperature, urinalysis, blood count, etc.

In the next, or "preservative" period, the chemical was administered, almost always by capsules taken during the meal, a method decided upon because of problems that arose with mixing the preservatives into the food. Lasting 15 to 20 days, this period was divided into three to five subperiods in which the dose would be increased.

In the third or "after" period, the same analyses and records were continued, and showed the rate of excretion of the chemical and return of the subject to a normal state. This was usually a 10-day period.

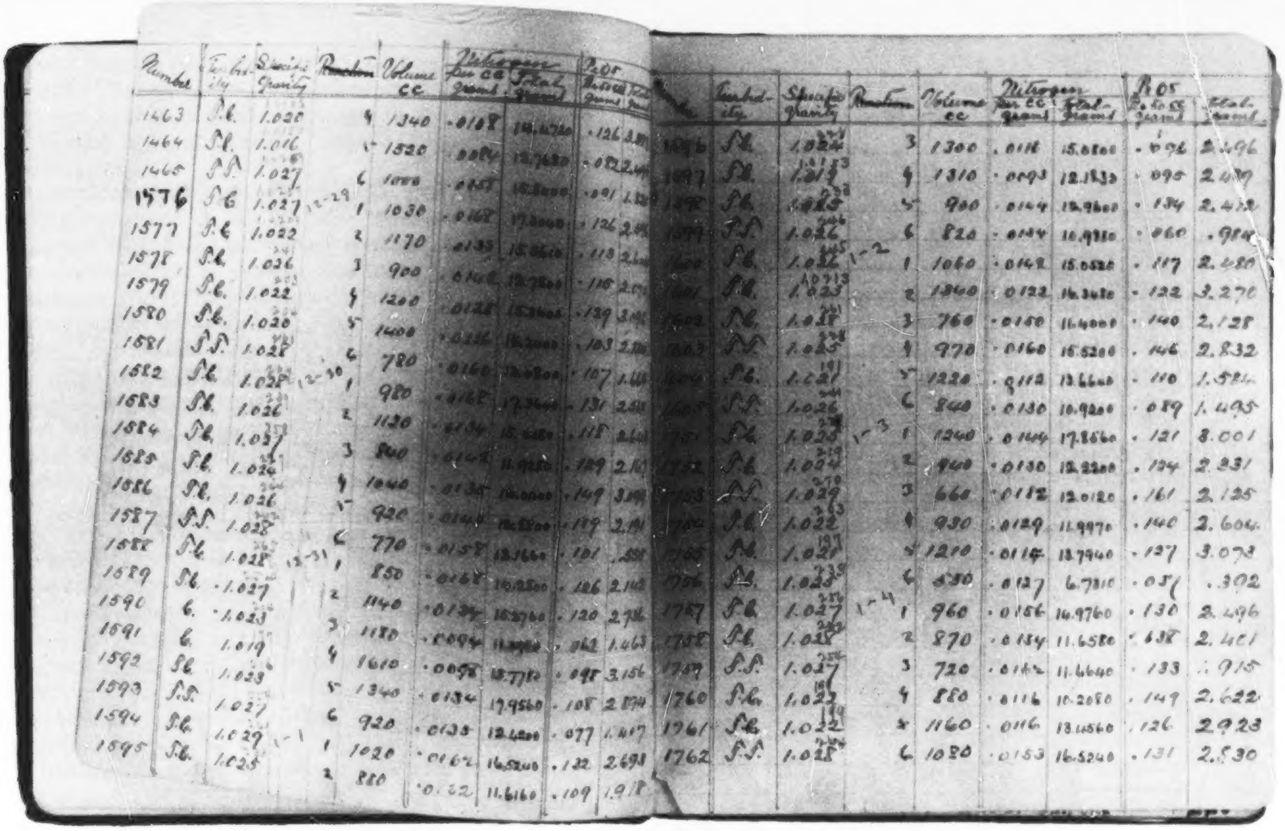
"Mental attitude" was seen by Wiley as having special importance in studies of digestion. "Cheerful surroundings, good company and in general an agreeable environment tend to promote the favorable progress of digestion. A reversal of the conditions, combined with mental depression, bad news and other unfavorable conditions, have exactly the opposite effect."

The young men were, of course, aware that chemical preservatives would be added to their diet. But how?

Borax and boric acid were the first chemicals tested because they were "probably the most important of the commonly used preservatives." In powder form, with little taste, considerable quantities could be mixed with food without being detectable. At first, the borax was administered in the butter—one of its principal commercial uses being to conceal rancidity. Soon, however, the members discovered that their butter contained the borax, and though it was hardly detectable by taste, "a dislike of butter was developed," and they ate less of it. Milk, meat and coffee were then tried as vehicles, with similar results. Finally, capsules were adopted for the rest of the experiments. Dissolution tests showed that the capsules, taken in the middle of a meal, would quickly release their contents into the food. Wiley reported that after this change no dislike developed for any particular food and in the case of borax no discomfort was noticed.

At first "small quantities" were given, "as much as would be consumed in eating foods preserved with borax. . . . these quantities were progressively increased so as to reach, if possible, the limit of toleration . . . by each individual." Dosages ranged from a half gram daily to four grams in the last subperiod.

Analyses of the foods and excretions, beginning with the "fore" period, continued to the end of the "after" period. Samples of the food and excretions were dried except for such foods as meats, fish and oysters. Special equipment was designed for drying the feces. Methods of the Association of Official Agricultural Chemists were used to determine the major nutritional indicators—water, nitrogen, phosphorus, fat and the heat of combustion (calories) for both the foods and the excretions. The latter, of course, were analyzed for boric acid content. Urinalyses were particularly important. They showed an increasing accumulation of borax in the system up to the fourth day, which then leveled off. Recovery of the chemical from the urine ranged from 86 to 94 percent of



Number	Turbidity	Specific Gravity	Reaction	Volume cc	Nitrogen Per cc gram	Nitrogen Total gram	P_2O_5 Per 100 cc gram	P_2O_5 Total gram
1463	S.l.	1.020	4	1340	.0108	14.4720	.126	[illegible]
1464	S.l.	1.016	5	1520	.0084	12.7680	.082	[illegible]
1465	S.S.	1.027	6	1000	.0158	15.8000	.091	[illegible]
1576	S.6	1.027	12-29 1	1030	.0168	17.3040	.126	[illegible]
1577	S.l.	1.022	2	1170	.0135	15.8610	.113	[illegible]
1578	S.l.	1.026	3	900	.0142	12.7800	.116	[illegible]
1579	S.l.	1.022	4	1200	.0128	15.3600	.129	[illegible]
1580	S.l.	1.020	5	1400	.0116	16.2000	.103	[illegible]
1581	S.S.	1.028	6	780	.0160	12.4800	.107	[illegible]
1582	S.l.	1.028	12-30 1	980	.0168	17.3640	.131	[illegible]
1583	S.l.	1.026	2	1120	.0134	15.0080	.118	[illegible]
1584	S.l.	1.027	3	840	.0142	11.9280	.129	2.16[illegible]
1585	S.l.	1.024	4	1040	.0135	14.0000	.149	[illegible]
1586	S.l.	1.026	5	920	.0140	12.8800	.119	[illegible]
1587	S.S.	1.028	6	770	.0158	12.1660	.101	[illegible]
1588	S.l.	1.028	12-31 1	850	.0168	14.2800	.126	2.142
1589	S.l.	1.027	2	1140	.0134	15.2760	.120	2.736
1590	6.	1.023	3	1180	.0094	11.0920	.062	1.463
1591	6.	1.019	4	1610	.0098	15.7780	.098	3.156
1592	S.l.	1.023	5	1340	.0134	17.9560	.108	2.894
1593	S.S.	1.027	6	920	.0135	12.4200	.077	1.417
1594	S.l.	1.029	1-1 1	1020	.0162	16.5240	.132	2.693
1595	S.l.	1.025	2	880	.0132	11.6160	.109	1.918

Number	Turbidity	Specific gravity	Reaction	Volume cc	Nitrogen Per cc gram	Nitrogen Total gram	P_2O_5 Per 100 cc gram	P_2O_5 Total gram
1596	S.l.	1.024	3	1300	.0118	15.3400	.096	2.496
1597	S.l.	1.013	4	1310	.0093	12.1830	.095	2.489
1598	S.l.	1.025	5	900	.0144	12.9600	.134	2.412
1599	S.S.	1.026	6	820	.0134	10.9880	.060	.984
1600	S.l.	1.022	1-2 1	1060	.0142	15.0520	.117	2.480
1601	S.l.	1.023	2	1340	.0122	16.3480	.122	3.270
1602	S.l.	1.028	3	760	.0150	11.4000	.140	2.128
1603	S.S.	1.025	4	970	.0160	15.5200	.146	2.832
[illegible]	S.l.	1.021	5	1220	.0112	13.6640	.110	1.584
[illegible]	S.S.	1.026	6	840	.0130	10.9200	.089	1.495
[illegible]	S.l.	1.023	1-3 1	1240	.0144	17.8560	.121	3.001
1752	S.l.	1.024	2	940	.0130	12.2200	.124	2.331
1753	S.S.	1.029	3	660	.0182	12.0120	.161	2.125
[illegible]	S.l.	1.022	4	930	.0129	11.9970	.140	2.604
1755	S.l.	1.021	5	1210	.0114	13.7940	.127	3.073
1756	S.l.	1.023	6	530	.0127	6.7310	.051	.392
1757	S.l.	1.027	1-4 1	960	.0156	14.9760	.130	2.496
1758	S.l.	1.028	2	870	.0134	11.6580	.138	2.401
1759	S.S.	1.027	3	720	.0162	11.6640	.133	2.915
1760	S.l.	1.022	4	880	.0116	10.2080	.149	2.622
1761	S.l.	1.022	5	1160	.0116	13.4560	.126	2.923
1762	S.S.	1.028	6	1080	.0153	16.5240	.131	2.530

Pages from one of the notebooks kept by members of the poison squad. This one records results of urinalyses.

the intake, with a rapid decrease in the "after" period. Traces were still detected for about eight days after dosage was stopped.

The amounts eliminated in the feces were found insignificant. A special study was therefore undertaken to find if the remaining borax was eliminated through perspiration. Two squad members dressed in "flannels" played tennis for several hours, then rode their bicycles for about an hour. "The temperature was high and the perspiration profuse." The water used for bathing and for washing the flannels was combined and then evaporated, and the residue analyzed. This produced a strong borax reaction, but the amount recovered was not enough for a quantitative determination by the methods then in use.

An attempt was also made to learn whether any of the chemical escaped in respiration. A squad member who had been receiving three grams daily for four days exhaled for three hours through a solution of lime water, which was then tested, with negative results.

Large quantities of information were tabulated for each squad member—from the notes of the doctors who did the weekly physicals, the forms and notes kept by the men themselves, and the analytical records. Wiley himself did most of the summarizing in the five study reports, published serially under the title "Bulletin 84," from 1904 through 1908.

The borax report, issued in 1904, set a pattern for the others.

The findings on borax were not impressive. Observations showed borax to be one of the least toxic of the preservatives studied.

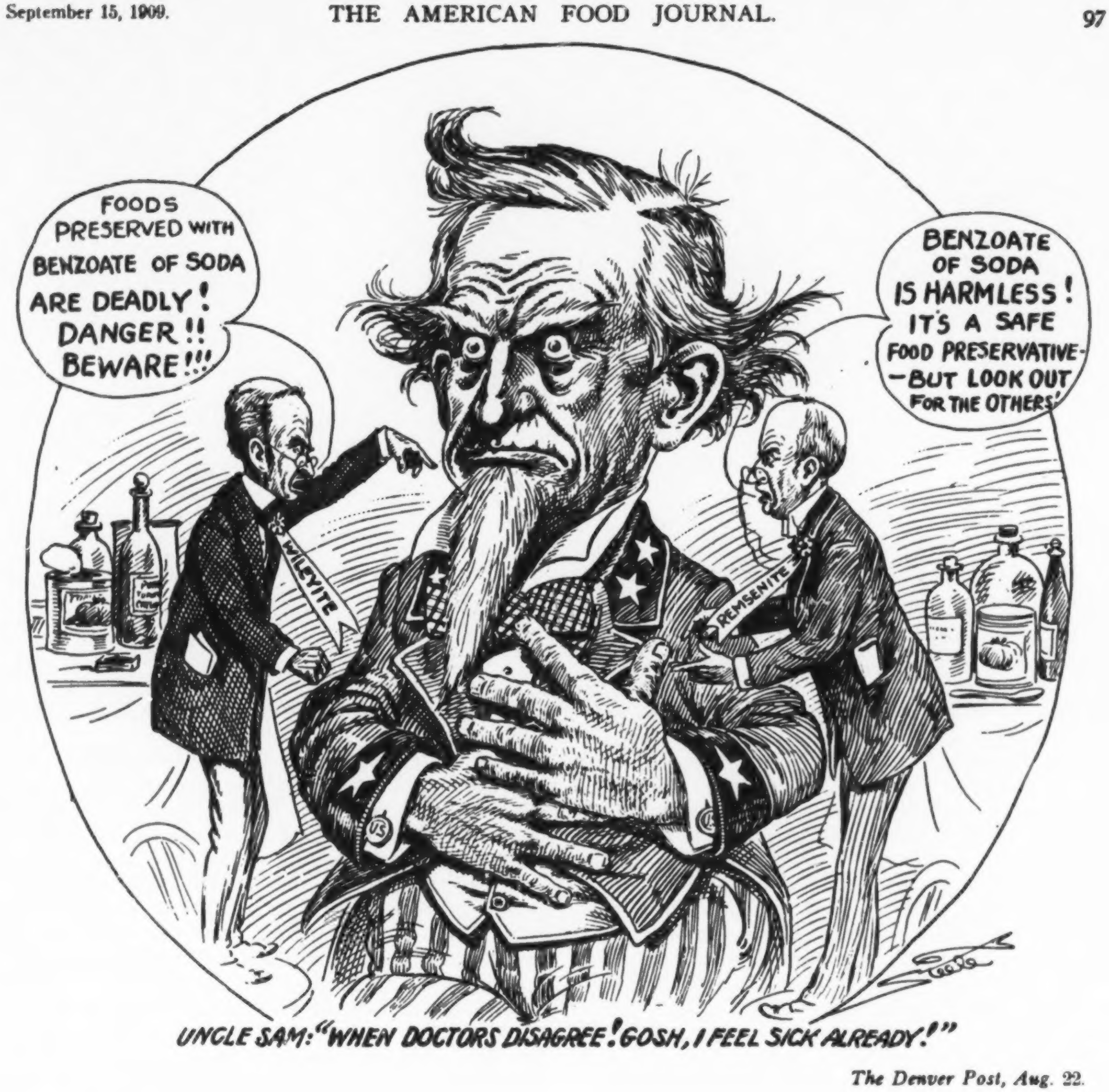
Average body weight of the men showed a "slight loss," with a tendency for this to continue in the majority of the subjects after dosage was stopped.

Blood examinations—not consistently performed, showed "a tendency to diminish the percentage of hemoglobin." Said Wiley: "The data must not be too literally construed because of their contradictory nature in regard to individuals. . . . If this preservative affects the number of corpuscles and the quantity of hemoglobin at all, it does so in a very irregular manner, differing in individuals, and in a way which cannot be used as the basis of any definite conclusion." Today, of course, blood studies would be given greater consideration.

Urine analyses showed slightly reduced nitrogen, increased acidity, a slight decrease in volume, and increased traces of albumin and microscopic material in the urine of some individuals. There was a "distinct tendency to increase the quantity of phosphoric acid excreted during the preservative period."

Total solids in urine showed a "marked decrease," with a "marked increase of solids in the feces." Fat metabolism appeared unaffected by the ingestion of borax, but it showed a slight tendency to "interfere with the combustion of food in the body," continuing into the "after" period.

More impressive were the symptoms reported in the individual case histories as dosage increased: diminished appetite, feelings of fullness and discomfort in the stomach, dull and persistent headache, and in some instances abdominal pain. There were no "notable effects" from low dosage (one-half gram daily) for a short period; i.e.,


September 15, 1909. THE AMERICAN FOOD JOURNAL. 97

FOODS PRESERVED WITH BENZOATE OF SODA ARE DEADLY! DANGER!! BEWARE!!!
WILEYITE
BENZOATE OF SODA IS HARMLESS! IT'S A SAFE FOOD PRESERVATIVE—BUT LOOK OUT FOR THE OTHERS!
REMSENITE
US

UNCLE SAM: "WHEN DOCTORS DISAGREE! GOSH, I FEEL SICK ALREADY!"

The Denver Post, Aug. 22.

Cartoon from The Denver Post *of August 22, 1909, during the 13th annual convention of the Association of State Food and Dairy Departments. Benzoate was a main issue of the meeting.*

occasional exposure, but a dose of one-half gram daily for as long as 50 days proved severe—"too much for a normal man." In the regular series of tests, the majority could ingest three grams daily and still perform their regular work but a four to five gram daily dose resulted in "inability to perform work of any kind."

Calculating that maximum exposure from all uses of the preservative would probably not exceed one-quarter gram per day, Wiley saw even this as too much of an added burden on the kidneys, notwithstanding the generally unimpressive data. Wiley concluded that borax should be banned as a food ingredient.

Wiley granted that very small amounts of preservatives might be harmless, as advocates had held, and might even protect consumers from more serious dangers from food spoilage, but he argued that the total of such additions was a danger to public health. He was convinced that any kind of regulation would have to treat all preservatives alike—apparently ruling out discrimination between food chemicals according to their risks and benefits.

The five leading food preservatives fed to the volunteers and reported on in Bulletin 84 were borax and boric acid, salicylic acid and salicylates, sulfuric acid and sulfites, benzoic acid and benzoates, and formaldehyde.

Each study produced a long, detailed report. There was some experimentation with other chemicals—the sweetener saccharin (also used as a preservative), potassium nitrate (for curing meats), and copper sulfate (used to color canned peas and other green vegetables).

Each of the preservatives studied was controversial and each was a story in itself. Although all the studies cannot be detailed here, at least the "score" of the final outcome can be given.

Formaldehyde was the first preservative involved in a Federal court action. No. 8 in the "Notices of Judgment" under the 1906 Food and Drugs Act reports the criminal prosecution of a milk shipper who adulterated his product with water and formaldehyde—"a poisonous and deleterious ingredient which rendered the milk injurious to health." Arraigned June 24, 1908, the defendant pleaded guilty and received a suspended sentence.

Eighteen months later, according to Notice of Judgment No. 224, U.S. marshals seized 144 30-pound cans of frozen liquid eggs containing formaldehyde, but also adulterated by "filthy, decomposed and putrid matter." The eggs had been consigned to a dealer in baker's supplies. The court ordered them destroyed.

While this case was in court, a more important one was being contested in the federal court at Peoria, Ill. This, too, involved liquid eggs, but the preservative was not formaldehyde but 2 percent borax. Attorneys for the egg company appealed on the ground that the eggs, seized in a cookie baker's warehouse, were no longer in interstate commerce. Important questions—whether the district court had jurisdiction and whether food ingredients held for further processing were covered by the new law—were decided by the U.S. Supreme Court, which ruled in favor of the government.

Not many court cases were aimed directly at the chemicals fed to the poison squad. Nevertheless, four are long gone from the food additive market—borax, salicylic acid, formaldehyde and copper sulfate.

Dr. Wiley did not win all his fights. As we know today saccharin is still in use as a sweetener, with appropriate labeling.

He also fed saltpeter to the squad, but no report was published. This form of the preservative (primarily potassium nitrate) has been almost entirely replaced by sodium nitrite, which continues to be permitted for curing meats, fish and poultry, and to prevent botulism.

Sulfuric acid in the form of sulfur dioxide gas, used as a fumigant to preserve the color of dried fruits and keep them from getting moldy, is now firmly classified as GRAS—generally recognized as safe.

Also GRAS is benzoate of soda, still permitted in the one-tenth of 1 percent concentration set in Wiley's Food Inspection Decision (FID) No. 76. This decision set an interim tolerance, announcing there would be no criminal prosecutions for use of benzoate in foods packed in 1907 and labeled to show the amount—a clear message that the chemical would eventually be banned. Fourteen months later FID No. 104 announced that a Referee Board of Consulting Scientific Experts had determined, from three separate and extensive investigations, that benzoate of soda mixed with food in small amounts (under 0.5 grams per day) "is not deleterious or poisonous and is not injurious to health." Benzoate was officially determined to be safe and the tolerance of FID No. 76 was made permanent.

What happened to bring about such a stunning reversal?

Sodium benzoate, while made synthetically, is a natural substance found in foods, notably the cranberry. Many food packers, especially of tomato products, were convinced it was necessary to prevent spoilage, notwithstanding that other packers had learned how to make superior products without it.

The pro-benzoate packers sought support at the highest level. The Referee Board, established to resolve such questions as the safety of benzoates, was composed of eminent scientists. Its members were selected by President Theodore Roosevelt from nominations by university presidents. Ira Remsen, president of Johns Hopkins, a co-discoverer of saccharin and considered the nation's outstanding chemist, was the chairman. His colleagues were Russell Chittenden, dean of Yale's Sheffield Scientific School; Christian Herter, of Columbia; John Long, of Northwestern; and Alonzo Taylor, of California.

Essentially, the board arranged to have Wiley's experiments repeated in three separate poison squad studies. In some respects the new studies improved on Wiley's design. They lasted longer, about two months. The dose range was greater, from 0.3 grams per day to a "large" dose of 0.6 grams to four grams. The chemical was diluted and actually mixed with the food instead of being given in capsules. The menus were more varied. The young men volunteers were not informed when the dosage began. Some additional tests and chemical determinations were made. And, of course, the subjects had not participated in previous investigations. In these differences may be clues as to why the results were so different.

Could poison squad studies be done today? Probably not. Extensive animal studies would be required by FDA regulations before using human subjects—in fact animal data would be relied on for much of the information required. This is not to say that human data would not be needed. A great deal of such data can now be obtained through systems of computerized medical reporting undreamed of in Wiley's time. The emphasis now would be on chronic toxicologic effects rather than acute or subacute effects. Evidence of carcinogenic, mutagenic and teratogenic effects would be sought. The physical examinations would be far more comprehensive. Females as well as males would be included in the program. Informed consent, other than a mere release from liability, would have to be documented. An institutional review board would monitor compliance with established guidelines for human experiments.

The poison squad studies were not undertaken for publicity purposes, but as it turned out, they played a major part in promoting the enactment of the 1906 law. The benzoate battle divided both the food trade and the public, with Wiley regarded as a zealot by some and a hero by others. Certainly his defeat on benzoates was one of the frustrations which led to his decision to retire from government service in 1912.

In any case, the results were far-reaching and beneficial. A beginning had been made in the scientific regulation of food additives, with rational limitations. Preservatives found safe could be legalized, but not to cover up the use of unfit ingredients.

Wiley had pioneered a scientific search for the facts, instead of relying on opinions, or on the absence of facts, or just waiting for them to turn up.

Wallace F. Janssen is FDA's historian.

The Kidneys: Complex Cleansing Units

by Judith Willis

What is shaped like a bean and produces a sterile liquid?

The answer is the human kidney, that vital, often overworked organ through which the body's blood is circulated every four to five minutes.

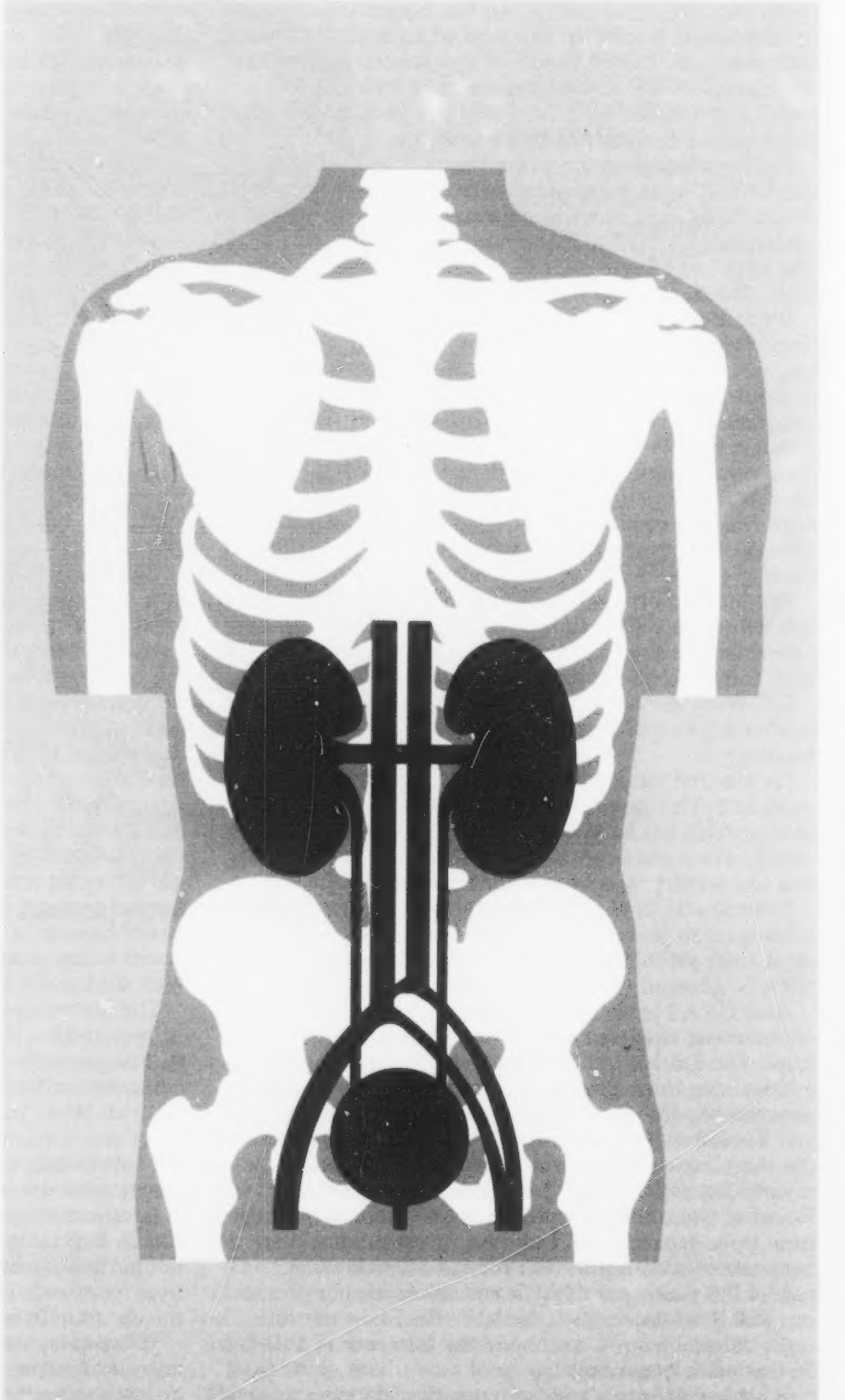
The bean-shaped kidneys, of which there are normally two in each person's body, lie facing one another on either side of the spinal column in back of the abdomen, just below the last rib. They are each four or five inches long by two or three inches wide, and one inch thick. Each weighs four to six ounces. The intestines are located on both sides of the kidneys and one adrenal gland lies over each. The liver usually pushes the right kidney down slightly lower than the left. The kidneys are cushioned by a pad of fat (called perirenal fat) that protects them from cold and injury and, together with blood vessels, helps hold them in the correct position. Extremely thin people may suffer from a condition known as ptosis, in which the kidneys drop because there is insufficient fat to hold them in place.

Contrary to popular belief, urine—the end waste product of the kidneys—is sterile. In a healthy person and in an emergency it could even be used to cleanse wounds.

Kidney function was once a riddle to which even wise old Aristotle couldn't find the correct answer. He thought that the kidneys were not vital organs, but rather that they added "a greater finish and perfection to the body." Urine, he believed, was formed in the bladder, not the kidneys.

It wasn't until the time of Galen, physician to Roman Emperor Marcus Aurelius in the second century A.D., that this concept was corrected. Galen correctly identified the kidneys as the organs in which urine is formed. He further identified the ureters (tubes leading from each kidney) as the conduits of urine, and the bladder as the organ of storage.

Kidney function was further illuminated in the 1600s by Lorenzo Bellini, who described the large papillary ducts in the kidney that bear his



name, and by Marcello Malpighi, who correctly described the kidney cortex (which previous anatomists had believed to be coagulated blood) as a compact mass of minute, tortuously coiled tubes connecting with the ducts of Bellini.

Each kidney consists of a solid portion and a cavity. The cavity is variously called the pelvis of the kidney or the pelvis of the ureter. The solid portion has two parts, the cortex and the medulla. The cortex is the outer part and is reddish-brown in color. It has a number of finger-like projections called "columns of Bertin," which extend to the medulla. Purplish in color, the medulla, or middle part of the kidney, contains eight to 18 pyramid-shaped structures and nephrons, or kidney tubules, which do most of the basic work of the kidney. There are approximately one million nephrons in each kidney. Each nephron begins in the cortex as an expanded, cup-shaped structure called "Bowman's capsule," which encloses a tuft of capillaries, called the glomerulus, arising from a branch of the renal artery, which brings blood to the kidneys.

Urine is formed in a three-step process of filtration, selective re-absorption and secretion. In the first phase, blood is filtered through the glomerular capillaries and Bowman's capsule. The filtering process leaves the red and white blood cells and platelets behind and pushes some of the liquid component of blood through the capillaries into the Bowman's capsule. The filtered fluid is similar to plasma in that it contains glucose, amino acids, salts, urea and uric acid in the same proportions as plasma, but much of the protein in the plasma is left behind.

While 150–180 liters (158–190 quarts) of fluid filter through the glomeruli of the kidneys each day, only about 1.5 liters leave the body as urine. The rest is returned to the bloodstream in a process called selective re-absorption. The nephrons are able to select what the body needs and return the rest to the bloodstream. Some substances, such as glucose, are usually re-absorbed fully. Others such as electrolytes are re-absorbed to a varying degree depending on the body's needs. Urine is about 95 to 96 percent water, and the rest urea, uric acid, creatinine, salts, phosphate, sulfate and metabolic end products. Urea, uric acid and creatinine are protein waste products.

Because of the kidneys' involvement in processing nutrients, adverse effects on them have been noted in persons on an exclusively protein diet. For example, electrolyte balance is endangered by a diet very high in protein to the exclusion of other nutrients.

Several hormones help the kidney to regulate re-absorption and secretion. Vasopressin, also called the antidiuretic hormone (ADH), is produced by the pituitary gland and is activated when the body's water content is diminished. Vasopressin stimulates water conservation, resulting in a highly concentrated urine. On the other hand, when a person drinks a large amount of water, ADH production is inhibited, and excess body water is excreted as dilute urine.

An abnormal and chronic lack or shortage of ADH results in a disease called diabetes insipidus. A person with this condition may excrete as much as two to three gallons of urine a day and, to compensate, must drink an equivalent amount of water.

Alcohol inhibits the release of ADH. This explains the common experience of frequent urination while drinking and the subsequent dehydration and thirst of the morning after.

Another hormone important to kidney function is aldosterone. Produced by the adrenal cortex, aldosterone regulates the rate and excretion of sodium and potassium and the water that carries these electrolytes. If the body is deprived of sodium, aldosterone is secreted and sodium excretion is reduced, producing a nearly salt-free urine; if excess sodium is ingested, aldosterone secretion is suppressed and a salt-rich urine is excreted.

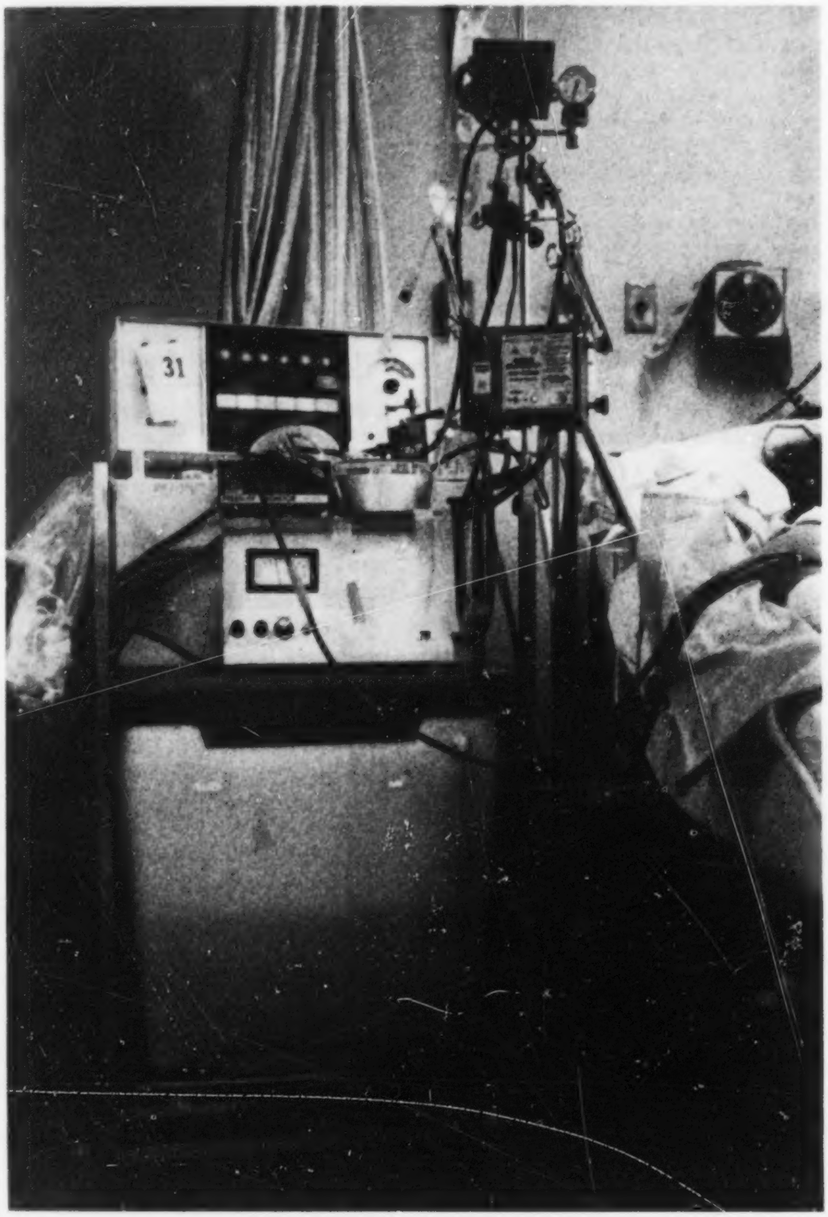
Prescription diuretics used to control high blood pressure or heart failure (Diuril, Exidrix and others) work by increasing the excretion of sodium and water.

Through the process of filtration and selective re-absorption and secretion, the kidneys maintain the body's fluids, electrolytes, acidity and alkalinity. In maintaining this balance, the kidneys also can influence blood pressure, and, in fact, abnormal kidney function often results in high blood pressure (secondary hypertension). Primary or essential hypertension, that is, high blood pressure not caused by abnormal kidney function, can apparently be controlled to a certain extent by blocking one of the major systems regulating high blood pressure, the renin-angiotensin-aldosterone system (RAA system). This can be done by treatment with a drug recently approved by FDA, Capoten (captopril).

Renin, an enzyme synthesized by the kidneys, activates the RAA system when it is released. Once in the bloodstream, renin acts on a substance called angiotensinogen to produce angiotensin I. Another agent, known as angiotensin-converting-enzyme (ACE), converts angiotensin I to angiotensin II. Angiotensin II elevates blood pressure by acting as a vasoconstrictor (blood vessel narrower) and by stimulating the secretion of aldosterone, which causes sodium and fluid retention. Capoten lowers blood pressure by interfering with this process.

The pigment that gives urine its usually pale yellow color is called urochrome. The color of normal urine, however, can vary from clear to brownish, and both the color and odor can be changed by certain foods. For example, eating a large amount of beets may give urine a reddish hue. Large amounts of asparagus may give urine the foul odor of methyl mercaptan, a substance that evolves during the digestion and metabolism of the vegetable. Urine of a diabetic may have a sweetish odor because it contains large amounts of sugar.

Sugar in the urine (glycosuria or



Kidney dialysis machine filters waste products from blood and returns cleansed blood back to the body.

glucosuria) can be an indicator of diabetes mellitus. Several other substances when found in the urine may indicate disease conditions. An abnormally high amount of protein, usually as albumin, in the urine (proteinuria), unrelated to exercise and persistent over a period of time, is almost always either drug-related or indicative of a kidney disease because it shows that the glomerulus is more "leaky" than normal, usually due to an inflammatory process. When present in the urine of a pregnant woman, albumin indicates pre-eclampsia, a dangerous condition involving abnormalities of blood pressure and kidney function. In a non-pregnant woman and in men, protein in the urine may indicate glomerulonephritis or nephrosis, serious kidney diseases. The presence of white blood cells or pus in the urine (pyuria) indicates infection.

Many drugs are processed in the kidneys and may have a number of effects on kidney function, including decreasing or increasing urinary output. Abnormalities of urination include painful urination (dysuria), which may indicate infection or obstruction; unusually large amounts of urine (polyuria), which may occur in diseases or as a side effect of some drugs; scanty amounts of urine (oliguria), which may indicate obstruction or disease, or may be drug-related; and absence of urine (anuria), usually related to an obstruction or serious malfunction.

The complex of symptoms that develops when the kidneys function very poorly is known as uremia. Symptoms include nausea, vomiting, anemia, high blood pressure, headache, chemical pneumonia, convulsions and dry yellowish skin. Uremia is the end result of any disease that reduces kidney function markedly.

Cystitis, a bacterial infection of the bladder, is more common in women than in men and is usually caused by bacteria that normally live in the intestines. Its symptoms include urinary urgency, frequency and burning during urination. It is generally treated with antibiotics. If cystitis is left untreated, infection can climb to the kidneys, where it is called pyelonephritis. This condition can also occur in the kidneys without a prior bladder infection. Pyelonephritis is especially common in diabetics, in pregnant women and in patients with kidney stones and other urinary obstructions. Symptoms include pain in the lower back and fever. Urinary urgency and frequency may not always be present in pyelonephritis. Symptoms may subside spontaneously but be followed by asymptomatic kidney infection. Antibiotic treatment usually clears the infection.

Sulfa, a drug commonly used to treat bladder and kidney infections, should be taken with large amounts of water. Its action places additional stress on the kidney, which may result in the formation of stones. However, with the newer, more water-soluble forms of sulfa, this is no longer as severe a problem as when the drug first came on the market several decades ago. Another drug often used to treat these infections, nitrofurantoin (Furadantin and Macrodantin) may turn the urine brownish.

Kidney stones are fairly common, occurring either as a result of medication or of other factors. They are usually composed of some form of calcium. However, patients with gout may have uric acid stones, while those with congenital cystinuria, excessive urinary secretion of the amino acid called cystine, may have stones composed of that substance. Most people do not have symptoms from kidney stones unless the stones pass from the kidney pelvis into the ureter. The intense pain from kidney stones is known as renal colic and occurs in the lower back, radiating into the thigh and groin of the same side. Stones may pass out with the urine or may become lodged in the urinary tract and require surgical removal. Stones in the ureter or bladder may cause inflammation and blood in the urine (hematuria).

Acute glomerulonephritis is a serious kidney disease that mainly affects children and young adults. It involves inflammation of the blood capillaries in the glomerulus and develops 10 to 14 days after a respiratory infection with specific strains of streptococcus bacteria. Its symptoms include sudden development of a wine-colored urine, fever, chills, loss of appetite, high blood pressure, swelling around the eyes or ankles and changes in blood chemistry. More than 85 percent of those who contact acute glomerulonephritis recover fully. However, 10 to 15 percent suffer from a continuing inflammation, chronic glomerulonephritis, that can lead to chronic kidney failure and may result in death.

Cancer of the urinary system most commonly occurs in the kidney and bladder. Kidney tumors may be quite large before they are detectable. One of the early signs of kidney cancer is microscopic amounts of blood in the urine sample. Bladder tumors are four times more common in men than in women and usually occur after age 50. The most common sign of bladder cancer is visible blood in the urine. There is a much higher incidence than average of this type of cancer in those who work with aniline dyes, benzene and naphthalene. There may also be a higher incidence among smokers. Early treatment is radiation or local surgical removal of the tumor. If treatment does not occur until later, complete removal of the bladder is necessary.

A person can live normally with less than one half of one kidney functioning. However, if both kidneys stop working, medical treatment is required or sickness and death will occur in a few days. The two types of treatment, hemodialysis and peritoneal dialysis, may be done in hospitals, dialysis centers or at home.

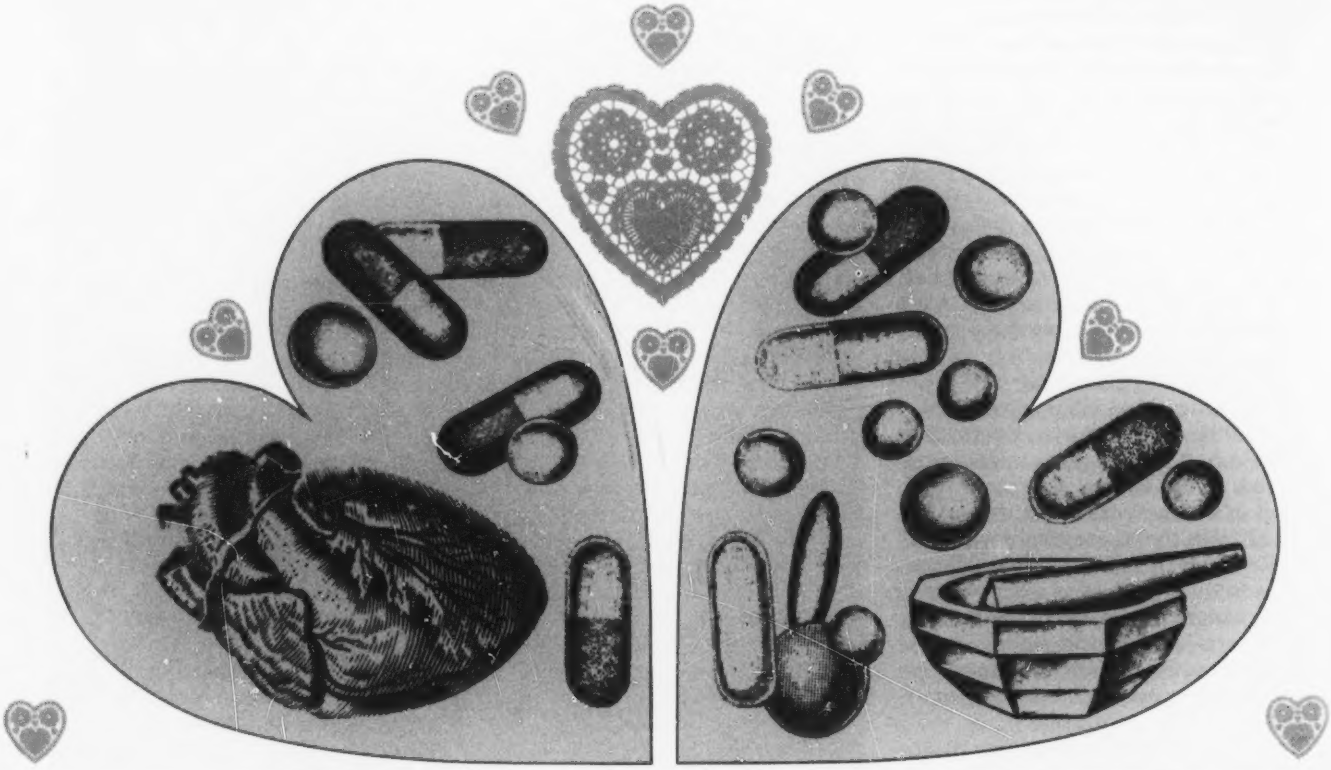
The hemodialysis machine functions as a kidney, filtering the waste products from the blood and returning the cleansed blood back to the body. In peritoneal dialysis, two liters of a special solution are instilled into the peritoneal cavity of the abdomen via a catheter. The waste products slowly diffuse into the solution that is later drained. Until a few years ago, peritoneal dialysis was not as commonly used as hemodialysis because it required that the patient be immobilized for a relatively long period. However, peritoneal dialysis has become more widely used with the recent FDA approval of collapsible plastic containers for the special solution used in continuous ambulatory peritoneal dialysis (CAPD), which allows patients to perform normal tasks while they are being dialyzed.

In the case of permanent failure of both kidneys, a transplant may be performed. The one year survival rate of transplant patients is now close to 90%, according to the American Society of Transplant Surgeons. The greatest success has been with transplants involving identical twins. Next most successful transplant is the kidney of a close relative. Transplants from non-relatives are least successful. Drugs and irradiation have been used to discourage rejection by suppressing the formation of antibodies.

A recent article in the Journal of the American Medical Association surmised that in the future fewer transplants will be given to patients now on dialysis because an increasing number have become sensitized to the foreign proteins that are likely to be found in a donor kidney, particularly one from other than a close relative. One study found that the proportion of sensitized patients grew from 32 percent in 1973 to 92 percent in 1977 and then leveled off. Reasons for this include increasing sensitization of patients to foreign proteins as a result of multiple blood transfusions in the pre-transplant period, and a growing number of prospective recipients sensitized from a prior rejected transplant. Two procedures, autoimmunization and radiation combined with bone marrow transfusions, may help to decrease the risk of rejecting a donor kidney, but the procedures are just in the investigational stage.

Judith Willis is editor of FDA's Drug Bulletin.

Drugs Are Dear To Many Hearts



by Annabel Hecht

When British physician William Heberden wrote his classic description of angina pectoris in 1772, he had little to offer his patients except quiet, rest, warmth and—as one author described it—"judicious use of opium." Rest and quiet are still beneficial in relieving this excruciating chest pain, but fortunately, today's physicians no longer have to rely on dangerous narcotics. They have a variety of far more effective drugs to give their patients for this and many of the other conditions that affect the heart and blood vessels.

Actually, angina pectoris is not a disease of the heart. Instead, it is a symptom usually associated with coronary artery disease. The coronary arteries are the blood vessels that supply blood to the heart itself. When these arteries become clogged with fatty deposits, a condition called atherosclerosis, the heart is deprived of the vital oxygen that is carried by the blood. The patient feels this loss, in the form of chest pain, on exertion and sometimes even when resting.

Dr. Heberden couldn't have chosen a more appropriate word to define this chest pain. Angina comes from the Greek *agkhone*, which means strangling and this is precisely the sensation patients feel. The pain can be made worse in situations when the heart's oxygen supply is decreased or its need for oxygen is increased. Cigarette smoking, for instance, can decrease the supply because it reduces the oxygen-carrying capacity of the blood. High blood pressure increases the heart's oxygen need because more effort is required to pump blood at high pressures. Physical exertion also increases the heart's demand for oxygen since the heart rate, force of contractions and blood flow must increase to meet the oxygen demands of other tissues.

The drugs used to relieve angina are aimed at reducing the heart's demand for oxygen. One group of drugs with this effect are the vasodilators, which work by relaxing blood vessels, causing them to dilate, or expand, enabling them to retain more of the blood that would normally go to the heart. This, in turn, reduces the amount of blood within the heart and reduces the heart's size. With less blood to pump, the heart has less work to do and thus needs less oxygen.

First choice for the immediate relief of angina is nitroglycerin, a vasodilator that has been in use for more than 100 years. A nitroglycerin tablet dissolved under the tongue can bring relief within a matter of minutes. More recent drugs of the same type—i.e., nitrates—include isosorbide dinitrate, erythrityl tetranitrate and pentraerythritol. The first two come in a form that can be dissolved under the tongue while all, including nitroglycerin, are available in a tablet that can be swallowed. A patient who expects to do something that requires exertion can use such a tablet to prevent angina for short periods. Nitroglycerin is also absorbed through the skin and when applied in the form of an ointment can improve the patient's ability to exercise for up to three hours.

Another vasodilator, not chemically related to the nitrates, is dipyridamole, used for preventive treatment of chronic angina. It does not provide immediate relief for acute pain.

At the present time, nitrates are also used to treat angina that occurs when the patient is asleep. This unusual type of chest pain, sometimes called variant or Prinzmetal angina, is caused by a spasm in a coronary artery.

Beta blockers are another type of drug that reduces the heart's need for oxygen. They are so called because they reduce, or block, certain stress effects on the heart. When the body is under stress, the hormone epinephrine is released by the sympathetic nervous system. Extra amounts of this hormone in the system increase heart activity and relax the smooth muscle of the bronchi, i.e., breathing tubes in the lungs. Two beta blockers, propranolol and naldol, are approved for the treatment of angina. In doing their job, these drugs reduce heart activity and thus the need for oxygen. At the same time, however, they constrict the bronchi, which means they should not be given to patients who also suffer from asthma.

Beta blockers are usually taken continuously to prevent rather than relieve angina attacks. This constant use can present problems, however, for when the speed and force of the heart's contractions are reduced, the patient may develop congestive heart failure. The name may suggest death is near, but congestive heart failure is actually a chronic condition that is the end result of many diseases affecting the heart. "Failure" in this sense means that the heart is unable to pump forcefully enough to deliver an adequate supply of blood to the body.

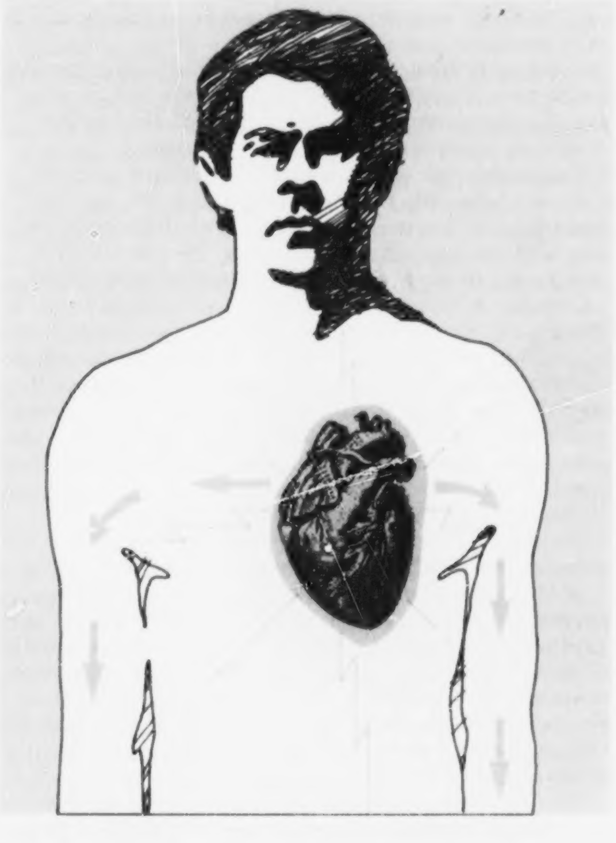
Congestive heart failure may involve either the right or the left ventricle (the pumping chambers of the heart) or both. If the left side of the heart is weakened, the right side pumps blood into the lungs faster than the left side can pump blood to the rest of the body. This causes the lungs to become swollen and congested, a condition called pulmonary edema. Shortness of breath is the primary symptom of left-sided heart failure.

If, on the other hand, the right side of the heart is weaker, blood will not be pumped into the lungs fast enough and blood and fluid will back up in the body causing swelling, or edema, particularly in the feet and legs. Diminished blood flow causes the kidneys to conserve water and salts in order to increase the volume of the blood and this leads to further edema.

The goal of drug treatment for congestive heart failure is to strengthen the heart's contractions so that it will pump more efficiently and to increase the excretion of salt and water to reduce edema. The drug to do the first job is digitalis, another "oldy but goody" whose history goes further back than nitroglycerin's. Digitalis is really a kind of generic name for a class of drugs called cardiac glycosides. Digoxin and digitoxin are the most frequently used glycosides.

Effective as they are, the cardiac glycosides have a number of drawbacks. For one thing, since they are eliminated slowly from the body, there is a danger that excessive amounts will build up in the system. They also can cause the heart to beat irregularly. Because the dose required for effective treatment is often very nearly the toxic dose, patients must be monitored carefully when they are taking digitalis-type drugs.

To do the second job of controlling edema, physicians prescribe diuretics, drugs that increase the output of salt and water in the urine. These are sometimes called "water pills." Chlorothiazide, spironolactone and furosemide are the generic names for some diuretics. There is one problem with diuretics—some of them do too good a job. Along with salt, other minerals such as potassium



The path of anginal pain, first described by Heberden in his classic treatise on this heart disease symptom, starts across the front of the chest, either at the upper, middle or lower end of the sternum (breast bone), from where it may spread across the breast into the left arm and at times into the right arm.

are eliminated from the body. This loss can be counteracted by taking potassium supplements, eating foods that are high in potassium, or taking a second diuretic that does not cause potassium loss.

Diuretics also are the first drugs used in the treatment of hypertension (high blood pressure), a form of cardiovascular disease that affects some 60 million Americans. Unlike other types of heart disease, there often are no symptoms associated with hypertension and the patient doesn't know he has it until his blood pressure is checked. Exactly what causes hypertension is not known but obesity, too much sodium in the diet, and a family history of the disease are all linked to it. What is known for sure is that untreated hypertension can lead to permanent damage, including stroke, kidney failure, blindness, congestive heart failure or heart attack.

In treating hypertension many physicians follow the "Stepped-Care Approach," starting the patient first on a diuretic to help rid the body of excess fluid and reduce the volume and amount of blood returning to the heart. If this does not do the job, additional diuretics and a drug that blocks the effect of the sympathetic nervous system may be added. Such a drug might be one of the beta blockers, or methyldopa, clonidine or reserpine. The third step in hypertension treatment is to add a vasodilator such as hydralazine or minoxidil. (For a more detailed description of the Stepped-Care Approach to hypertension see *The Story Behind Those High Blood Pressure Readings*, in the May 1981 FDA CONSUMER.)

Drugs also play a role in controlling irregularities of the heart beat called arrhythmias. At rest, the normal heart beats at a rate ranging from 60 to 100 beats a minute, with the average about 70 beats. This steady pace is maintained by impulses sparked by special cells, called pacemaker cells, within the heart muscle. Disturbances in rhythm can involve the pacemaker cells themselves or the conduction system that carries the impulses to the rest of the heart. The result can be too slow a heart beat (less than 60 beats per minute), called bradycardia; too fast a beat (over 100 beats per minute), called tachycardia; and sometimes, wild, uncontrolled heart beats, called fibrillation.

These disturbances can be corrected by drugs that block the abnormal conduction of impulses or that restore normal conduction. Among those that achieve the first effect are quinidine (which, as its name implies, is related to quinine), procainamide, disopyramide and propranolol. Although digitalis-type drugs can cause arrhythmias, they are also used for long-term treatment of these irregularities. Phenytoin, a drug usually associated with the treatment of epilepsy, is the only drug given orally to restore normal conduction and is used to correct arrhythmias caused by too much digitalis.

The newest drug on the American scene to combat heart irregularities is verapamil, one of a group of drugs called "calcium slow channel blockers." Considered one of the most important therapeutic advances of the decade, the slow channel blockers act by decreasing the movement of calcium in the cells of the heart's conductive tissue. (Calcium plays a part in stimulating the contraction of all muscles in the body.) Slowing the movement of calcium inhibits or abolishes unwanted electrical stimulation, resulting in a slower heart beat. At present, verapamil is available only in intravenous form.

Diseases of the vascular system—the arteries and blood vessels—are usually chronic conditions that have developed over time. In the arteries, deposits of cholesterol can build up causing the vessels to become narrowed or blocked, thus reducing the flow of blood to various parts of the body. The result may be a stroke if the arteries bringing blood to the brain become clogged; or it may be angina or heart attack if the arteries bringing blood to the heart are involved. The main problem that can develop in the blood vessels is the formation of clots that cause inflammation and swelling. If the clots break loose, they may travel to the lungs or block vital blood vessels in other areas such as the brain.

Clofibrate, nicotinic acid and cholestyramine are drugs used to lower the cholesterol levels in the blood. However, because they do have serious side effects they are usually used only after other cholesterol-lowering efforts, including appropriate diet, exercise and weight reduction, have failed.

Anticoagulants, such as warfarin and dicumarol, are prescribed to prevent the formation of blood clots. They do their job by blocking the body's ability to use vitamin K, an essential element in the clotting process. There is always the danger that such drugs may interfere too effectively with this process and that serious bleeding may result.

Another anti-clotting drug is the old family stand-by, aspirin. What aspirin does is prevent the binding together of platelets, tiny blood cells whose function is to prevent blood loss by sealing off breaks in the blood vessels. Platelets sometimes clump together to cause blood clots. Early in 1980, FDA reported that aspirin's anti-clotting effect helped prevent recurrent transient ischemic attacks—little temporary strokes—in men.

Thanks to the variety of drugs now available, people who suffer from cardiovascular diseases do not have to become lifetime invalids. But because many forms of these diseases are chronic, those who suffer from them will have to take one, possibly several, drugs for the rest of their lives. For this reason it is important to follow these basic rules:

- Learn the name of each medicine prescribed and the reason why you are taking it.
- Follow the doctor's orders carefully. Do not change the amount of drug you take or the time at which you take it. Taking drugs at random intervals can interfere with their effectiveness and may even be dangerous.
- Renew prescriptions in time to avoid interruptions in dosage schedule. Some drugs, such as diuretics, can be purchased in large amounts, but others, such as nitroglycerin, lose their strength if kept too long.
- Never use another person's prescription even if your symptoms are the same. The dosage of some heart drugs is tailored to fit each patient's own needs.
- Some drugs interfere with the actions of others. Always check with your doctor before taking any medication he or she did not prescribe for you.
- Keep each medication in a separate container, with the name of the drug and the directions for use clearly marked. Nitroglycerin must be kept in a container that does not let in light.
- Always keep drugs out of the reach of children.

Annabel Hecht is a member of FDA's public affairs staff.

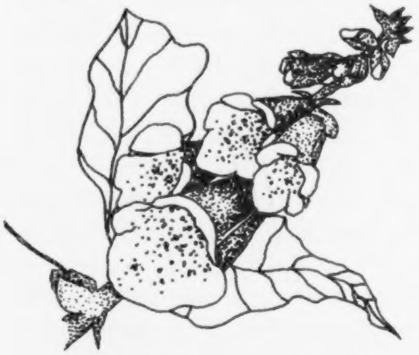
Why the Drugs Went to the Heart

Most of the drugs used in the treatment of cardiovascular diseases are products of the 20th century and many of these have come on the market only in recent years. But three drugs that are among the mainstays of therapy have histories that go back several centuries.

Digitalis. One of the most well-known of modern drugs that came from plants is digitalis, a derivative of foxglove. The botanical name, Digitalis purpurea, was assigned by Fuchsius in 1542 because the blossoms resemble the fingers of a glove.

Digitalis gained medical recognition through the work of an English physician, William Withering. In 1775 Withering was given the recipe for an herbal tea used by an old country woman to treat recalcitrant cases of "the dropsy," a condition now known as edema. Being a student of botany as well as of medicine, Withering was able to identify foxglove as the active ingredient among the 20 plants in the old woman's concoction.

For 10 years, Withering studied and experimented with foxglove before publishing his ACCOUNT OF THE FOXGLOVE AND SOME OF ITS MEDICAL USES. In it, he described the drug's more obvious effects, including increased urine flow, nausea and purging. Although he could not have known at that time that the principal effect of the drug was on the heart, he recognized that it had "a power over the motions of the heart."



In the early years of the 20th century digitalis was regarded as a specific treatment for fibrillation. Only in the last 60 years has it been established that the main value of the drug is in treatment of congestive heart failure.

Quinidine. Even before Withering began his investigation of foxglove, a Paris physician, Jean-Baptiste de Senac, made an interesting observation about a drug not usually associated with the treatment of heart disease. In 1749 he reported he had used powdered cinchona bark to cure "rebellious palpitation" of the heart. Cinchona, the source of quinine, had been introduced in Europe in the 17th century as an anti-pyretic (fever reducer) and anti-malarial.

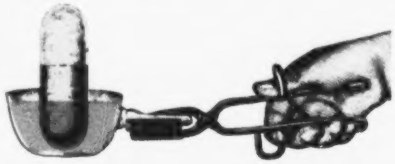
De Senac's observations were ignored and it was more than 150 years before cinchona bark was recognized as a potent drug for the heart. Oddly enough, it was a patient and not a physician who made the discovery. It happened in 1912 in Vienna. A patient came to a Dr. Karl Wenckebach complaining of an abnormal heartbeat. When the doctor said he could not promise a cure, the patient declared he would cure himself. This he did with massive doses of quinine.

This seemingly unorthodox use of the anti-malarial drug led others to take a closer look at quinine, cinchona and quinidine, a chemical cousin of quinine that had been around since Pasteur's day. Quinidine was found to be the most effective and is now one of the drugs of choice in treating heart irregularities.

Nitroglycerin. Unlike digitalis and quinidine, nitroglycerin comes not from plants, but from the chemist's laboratory. The arrival of this drug on the medical scene is actually the second part of the story. First came amyl nitrite, a volatile liquid synthesized in 1844. Early investigators reported that amyl nitrite caused flushing of the face, throbbing of the arteries in the neck and increased heart rate. One physician, however, noted that the drug also lowered arterial tension. Thomas Lauder Brunton, a young Scottish medical student, observed some of these experiments and decided to test the effects of amyl nitrite on angina.

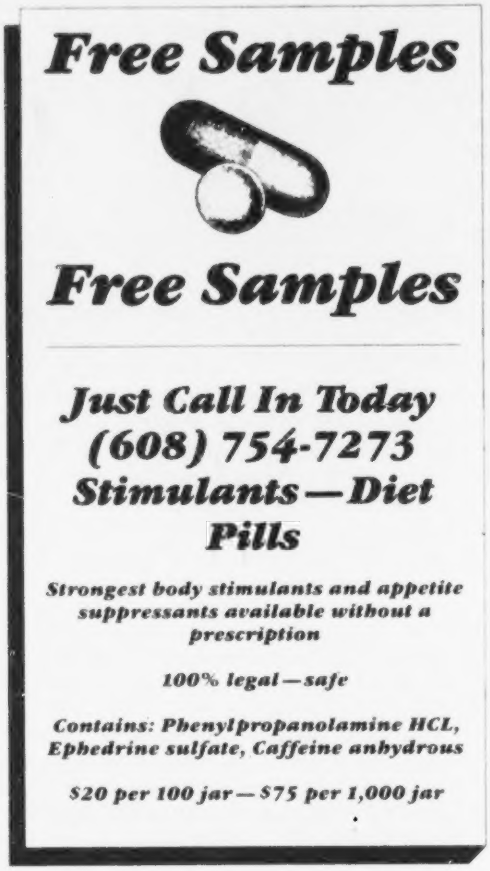
Brunton asked his patients to inhale the drug from a cloth on which he had poured amyl nitrite. Within a minute he observed that, along with the flushing of the face and drop of blood pressure, their chest pains disappeared. Brunton's paper On the Use of Nitrite of Amyl in Angina Pectoris was published in the British medical journal LANCET in 1867.

Twenty years later, William Murrell, then a lecturer in physiology at London's Westminster Hospital, became intrigued by a number of controversial reports of the effects of nitroglycerin he had found in some old medical journals. He decided to try the drug on himself. Despite some rather excruciating side effects, including a pounding heart and a throbbing headache, Murrell gave himself nitroglycerin about 40 times. He also gave the drug to several friends who experienced similar effects. At the same time, several claimed they had obtained relief from long-standing neuralgia pains.



Murrell saw a similarity between the effects of nitroglycerin and those reported for amyl nitrite and concluded that the drug might be useful in treating angina. He administered it to three patients as a 1 percent nitroglycerin solution in half an ounce of water three times a day and found that it not only reduced the number of attacks of angina they experienced, but also that it provided relief when taken during an episode of pain. Murrell's paper Nitroglycerin as a Remedy for Angina Pectoris was published in the LANCET in 1879. Today, nitroglycerin is the drug of choice for relieving acute episodes of anginal pain.

On The Trail Of Counterfeit Drugs



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100% legal—safe

Contains: Phenylpropanolamine HCL, Ephedrine sulfate, Caffeine anhydrous

$20 per 100 jar—$75 per 1,000 jar

—Excerpted from an advertisement in Cosmopolitan *magazine.*

[Brother] informed me that [deceased] was in good physical health, that he was a construction worker, that he did not take drugs, not even aspirin but that he did drink [both beer & mixed drinks]. [Brother] stated that their mom had high blood pressure & was diabetic & under a doctor's care . . .

According to [the attending physician], the story as told to him from friends of the deceased was as follows. [Deceased] was out with friends the evening of 12/26/80 in Albuquerque. He supposedly drank several shots of bourbon & took two black capsules from a lady friend who is known to take narcotics. [Deceased] & his male friends went to one of the friends' homes around 4 a.m. on 12/27, ate breakfast and went to bed. Around 6:30 or 7:00 a.m. the friends were awakened by gagging & gurgling noises. They found [deceased] on the floor, he had vomited, and was blue & cyanotic. They cleared his airway, attempted to arouse him & when he did not respond, they drove him to St. Joseph's [hospital]. At the time of admission, [deceased] was cyanotic & deeply comatose; a hemorrhage could be seen in the right retina. According to [the attending physician], the deceased was treated for drug overdose, a check was run for Doriden, which was negative. Toxicological screen showed ephedrine = 3 mg/ml.

On 2/13/81 I talked with William Slease with the Office of Medical Examiners. He stated that the cause of death was cerebral hemorrhage due to an aneurism. This aneurism could have burst for a number of reasons, physical exertion, sexual activity, etc. anything which would raise the blood pressure. He also stated that the legal stimulants would have also increased the blood pressure but that he did not know if he could show a direct association. . . .

—From an FDA investigator's report

* * * *

"I'm not going to quit. I like making the money. And I'm filling a need. . . .

"You don't see any damned labels or warnings on a bottle of whiskey, mister. I don't want to hear that crap. I've heard it too long. Gun dealers are the same thing. A guy goes out and blows his old lady away; that's not the gun dealer's fault. That's the idiot that pulled the trigger."

—Jerry Hecht, an OTC look-alike drug dealer from Albuquerque, N.M., in separate interviews on ABC and CBS television.

* * * *

The problems posed by these products include the following:

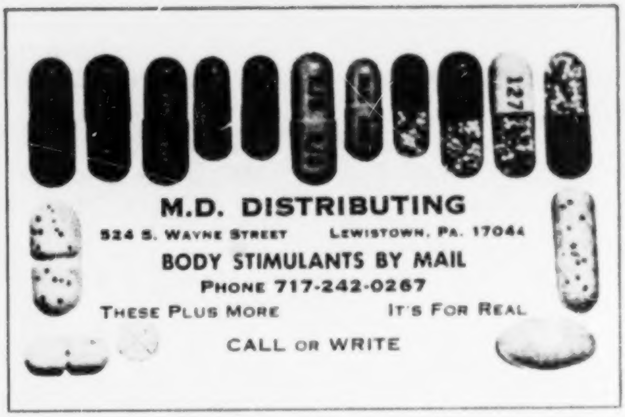
1. They induce a population of school children and others who do not usually abuse drugs to do so.

2. They counteract drug abuse educational programs by fostering the false notion that these products are legal and safe.

3. They give those who take them the impression that the real amphetamines, diet pills, methaqualone, etc., are not as potent and dangerous as they really are.

4. By flooding the street with cheap imitations, they confound DEA [Drug Enforcement Administration] and police efforts to deal with the real drugs of abuse.

—From a memo signed by the deputy director of FDA's Bureau of Drugs, Jerome Halperin.



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THESE PLUS MORE IT'S FOR REAL

CALL OR WRITE

Look-alike drugs have been advertised to college students via cards such as this, left under the windshield wipers of a car parked at the University of Maryland.

* * * *

Phenylpropanolamine (75 mg) and caffeine (220 mg) capsules in bottles of (60) (Time release diet capsules) Twelve bottles per case $50

Ephedrine sulfate (25 mg) and caffeine (200 mg) capsules or tablets (specify) bottle of 1,000 (Body stimulant and decongestant) $50

—From an ad by Clifton Pharmacal Wholesale, Inc., Milroy, Pa.

* * * *

"I really think what we're doing is a public service. People look at me and see the Harley-Davidson [motorcycle] jacket and think I'm out to cause trouble, but I don't bother anybody. I'm doing some good for this town. How? I'm putting [illegal] drug dealers right out of business."

—OTC look-alike drug dealer James Munson of Cedar Rapids, Iowa, quoted in the DES MOINES REGISTER.

* * * *

V.I.P. Pharmaceutical Inc., Pearl River, N.Y.

This is a contract manufacturer of OTC look-alike products. Four samples were collected as follows:

a. A black capsule marked "RJS" on both halves mimics Biphetamine 20 (See *discussion under Newtron Pharmaceutical Inc.).*

b. A white bisected tablet marked "LEMON 747 Cal." Quaalude is a white single-scored tablet with "LEMON 714" imprinted on its surface.

c. A pink heart-shaped tablet (a possible mimic of Benzedrine).

d. A yellow capsule with both halves marked "18-879." (Ionamin 30). . .

Tooling for the "LEMON 747 Cal" and heart-shaped tablet product were noted on the premises. The empty shells for the black capsule are marked with "RJS" logo with a machine located on the premises.

—From an FDA inspection report

* * * *

. . . By means of such activities and through the use of these and similar promotional materials. Respondent represents, directly or indirectly, in substance and effect, whether by affirmative statements, implications or omissions, that:

(a) The drug products involved may be safely used by the general populace.

(b) The drug products involved are prepared, labeled and marketed in accordance with the Federal Food and Drug laws. . . .

4. The aforesaid presentations are materially false as a matter of fact.

—From a United States Postal Service complaint filed Aug. 31, 1981, against 39 OTC look-alike distributors seeking to stop delivery of mail to the firms.

* * * *

At the request of the Food and Drug Administration and the Department of Justice, U.S. marshals today seized fake pep pills and other non-prescription "look-alike" drugs at factories in New York, Illinois, Pennsylvania, Florida and Alabama. . . .

Some of the products seized are similar in size, shape, color and markings to 'uppers'—amphetamine products such as Biphetamine-20 and Ionamin 30 that are often diverted to street sales. The counterfeit pills, however, usually contain a combination of non-prescription ingredients such as caffeine, phenylpropanolamine [a nasal decongestant and appetite suppressant] and ephedrine [a decongestant].

Other products seized look like "downers"—prescription sedatives such as Quaalude-300 or potent narcotic analgesics like Dilaudid. These also contain one or more non-prescription drugs such as antihistamines. . . .

The marshals seized the look-alikes at nine manufacturers:

V.I.P. Pharmaceutical Inc., Pearl River, N.Y.; Newtron Pharmaceutical Inc., Coram, N.Y.; Pharmadose Inc., Hauppauge, N.Y.; Jerome Stephens Pharmaceuticals, S. Central Islip, N.Y.; L.N.K. International Inc., Hauppauge, N.Y.; Standard Pharmacal Corp., Elgin, Ill.; Valley Run Pharmaceutical Corp., Milroy, Pa., [doing business as Clifton Inc.]; B.T. Products Inc., Tampa, Fla.; Frye Pharmaceuticals Inc., Birmingham, Ala.

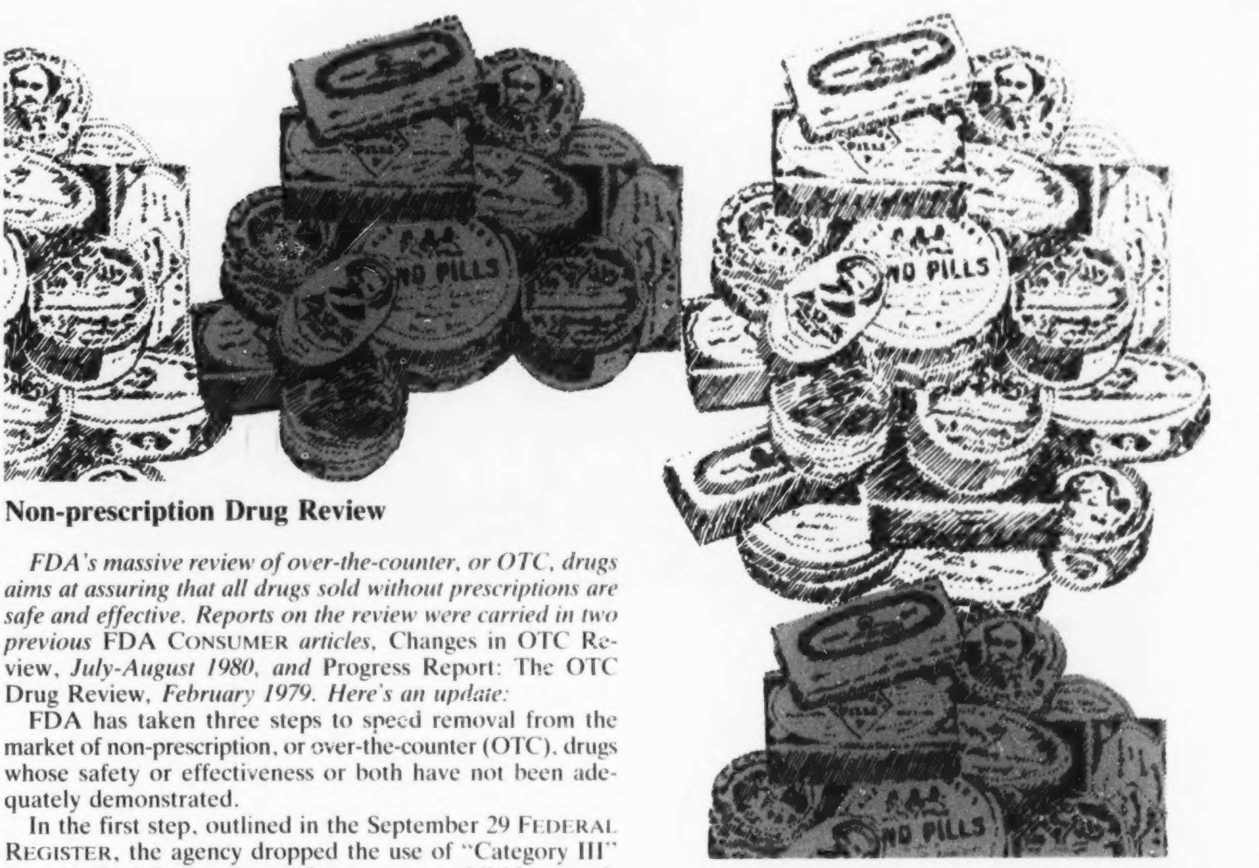
FDA has encouraged and supported state attempts to deal with this problem. Currently, 13 states have passed legislation banning distribution of these counterfeit drugs and others have similar legislation under consideration. The 13 are Delaware, Indiana, North Carolina, Oregon, Kansas, Maryland, South Dakota, Arkansas, Florida, Colorado, Louisiana, Oklahoma, and Connecticut. . . .

The seizures netted approximately 15 million filled capsules and manufactured tablets, many packaged and ready for sale, and more than 20 million empty capsules imprinted with the counterfeit markings. The marshals also seized machinery used in the manufacture of the counterfeits, including punches, dies, imprinters and presses. The machinery has been valued at over $1 million.

—From a Sept. 30, 1981, FDA news release.

Compiled by Roger W. Miller, editor of FDA CONSUMER

Updates



Non-prescription Drug Review

FDA's massive review of over-the-counter, or OTC, drugs aims at assuring that all drugs sold without prescriptions are safe and effective. Reports on the review were carried in two previous FDA Consumer *articles,* Changes in OTC Review, *July-August 1980, and* Progress Report: The OTC Drug Review, *February 1979. Here's an update:*

FDA has taken three steps to speed removal from the market of non-prescription, or over-the-counter (OTC), drugs whose safety or effectiveness or both have not been adequately demonstrated.

In the first step, outlined in the September 29 Federal Register, the agency dropped the use of "Category III" from its final drug monographs, reports establishing standards for OTC drugs. Category III included ingredients for which further evidence of safety or effectiveness or both was needed.

In the second step, the agency is establishing tougher deadlines for the time that certain ingredients in a drug can remain on the market after FDA issues a final monograph for that particular drug category. Under the old procedure, manufacturers were given as long as two years after publication of the monograph for marketing those drugs thought to be probably safe and effective on the basis of long use, so long as the manufacturers were conducting further tests.

Under the new procedure test data for Category III ingredients must be submitted by the time the final monograph is issued. When the final monograph is published, only drugs found both safe and effective may remain on the market. Those found ineffective or unsafe or needing further study must be removed. The purpose of these two steps is to assure that non-prescription drugs won't linger on the market after FDA concludes that additional proof is needed of safety or effectiveness or both.

In the third step, FDA said it would act more quickly to remove from the market some drugs found either unsafe or ineffective. Under the old procedure such ingredients were removed only after an additional period for public comment.

The new policies affect the procedures in FDA's massive review of all non-prescription drug ingredients, begun in 1972. In the review, 17 panels of experts placed ingredients that were under review in one of three categories: Category I—safe and effective; Category II—not safe and ineffective; Category III—sufficient proof of safety and effectiveness does not exist and further testing is needed.

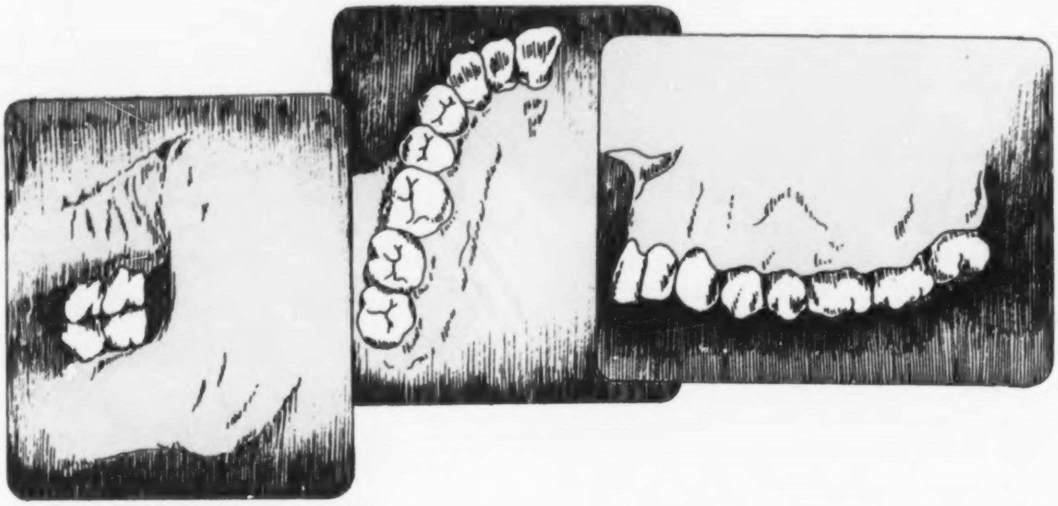
In a court case filed in the U.S. District Court for the District of Columbia in 1978, the Health Research Group, a consumer advocacy organization, challenged the practice of permitting the continued marketing of Category III ingredients after issuance of a final monograph. In a July 1979 decision Judge John J. Sirica, although he did not rule Category III to be illegal, said FDA could not explicitly exempt drugs in this category from regulatory action after a final monograph is issued.

The new policies, proposed in May 1980, became effective November 28.

Subscription Price Increased

For the second time in less than six months, the Government Printing Office has ordered a price increase for *FDA Consumer* magazine. The new price is $17 a year delivered in the U.S. and $21.25 for foreign delivery.

The Notebook



The Notebook: a potpourri of items of interest to consumers, gathered from FDA press releases, FEDERAL REGISTER *notices, and other news sources. Publication dates of* FEDERAL REGISTER *items, designated FR, are included to guide readers who want further information.*

■ Valium, once the country's **most prescribed drug,** has dropped to fourth place, according to Pharmaceutical Data Services. Topping the list of drugs most often prescribed in the first half of the year were Tagamet, an ulcer drug; Inderal, an anti-hypertensive and Motrin, an anti-arthritic/analgesic. In fifth place was Dyazide, a diuretic.

■ Blood banks should continue to use existing **color codes for blood** product labels until FDA makes a final decision whether to change the color code system. Last year the agency encouraged voluntary use of labels that comply with proposed revisions in requirements. However, proposed ABO color coding was not to be used optionally for two years after publication of the final rule. Because of objections to the new color code, FDA warns there may be revisions in the final guidelines and color labels prepared under the proposed rules may be unacceptable under the final regulation (FR September 29).

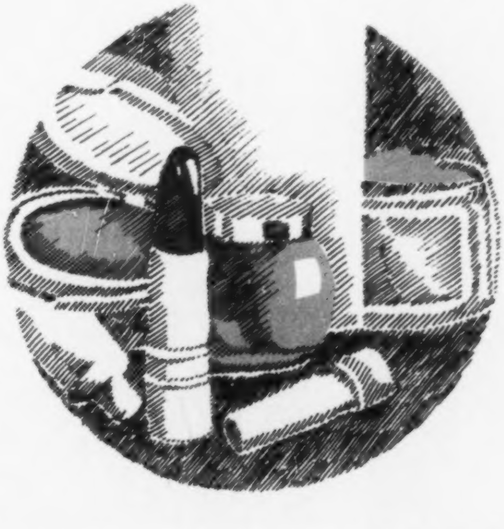
■ **Dental X-rays** should not be made routinely for detection of cavities, but only after a thorough clinical examination and review of the patient's dental history, including previous X-rays. This recommendation came out of a Technology Assessment Forum held last summer to promote the safe and effective use of dental X-rays. The forum was sponsored by the National Center for Health Care Technology of the Public Health Service.

Forum participants also recommended that clinical instead of X-ray examination be used initially to detect periodontal diseases, but said X-rays may be needed to diagnose conditions such as unerupted teeth and developmental abnormalities. Dentists should not take X-rays to provide protection against malpractice suits or to educate students, or because the patient asks for them.

■ Under a program that began October 1, FDA is furnishing information about **drug product quality** to states for use in awarding contracts for drugs. Delaware, Pennsylvania, Florida and Rhode Island are the first to request the information, which confirms that drugs to be purchased (and their manufacturers) have met agency requirements as well as all process standards and product specifications. New York state reported a significant reduction in drug procurement costs during a pilot test of the program. Participating states received the same drug quality information that has been provided since 1975 to federal agencies that contract for drugs.

■ FDA is allocating approximately $1 million this fiscal year to support research on **drug use** and possible **adverse effects** of marketed drugs. The agency issued a request for applications in October to encourage development of research projects in the area of drug-induced illness. Support will be in the form of cooperative agreement awards averaging from $300,000 to $400,000. Awards are expected to be made beginning in February 1982 (FR October 6).

■ FDA's **color additive regulations** have been amended to permit grape extract to be used as a color additive in non-beverage foods. At the same time, the closing date for the provisional listing of D&C Green No. 6 for use as a color additive in externally applied drugs and cosmetics was postponed from September 29 to December 1, allowing time for completion of FDA's review and evaluation of data on external uses of the color (FR September 29).



■ FROM OTHER REGULATORY AGENCIES: The Drug Enforcement Administration has issued final regulations permitting the transfer of **prescription information** between pharmacies for controlled substances prescriptions that are lawfully refillable. The rule, effective October 5, is expected to reduce health care costs to patients (FR October 5). . . . **Alpha-methylfentanyl** has been placed in Schedule I of the Controlled Substances Act by DEA. The opiate drug has been associated with numerous drug overdose deaths (FR September 22). . . . The Civil Aeronautics Board has revised its rules on **smoking on aircraft** to require all certified and commuter airlines with more than 30 seats to separate smokers and non-smokers and to provide a seat in the no-smoking section for all non-smokers who arrive by the airline's check-in deadline. Originally the smoking rules applied to certified air carriers only and airlines had to accommodate all non-smokers regardless of when they arrived for boarding. The review of smoking rules was begun in February 1981 when CAB raised the possibility of prohibiting all in-flight smoking or abolishing all CAB smoking regulations (FR September 16).

Investigators' Reports

The Show Must Not Go On

by Carol Ballentine

The lights dimmed, the music rose into clearly recognizable strains of a pop song, and the audience leaned forward, eager, waiting. Suddenly an array of patterned lights exploded in a myriad of colors and shapes, a symbiosis of the Fourth of July and a cosmic awakening. The laser light show had begun.

As the patterns shifted on the ceiling of the Soho loft theater in New York City, members of the audience gave themselves up to the sensory experience. The show, put on by Laser Physics, Ltd., and Basic Lighting, Inc., of New York City, included a sweep of brilliant light across the audience. Many in the crowd thought it just another entertaining part of the show. But at least one spectator was alarmed, possibly remembering some warning about the dangers of the extremely concentrated light produced by lasers. The spectator was also savvy enough to know whom to call about the problem—FDA's Bureau of Radiological Health.

Laser light shows were first introduced on the American entertainment scene in 1973 in Los Angeles. Since then, the shows have delighted audiences across the country. But the spectacular visual displays—frequently used to enhance music at concerts, discotheques and planetariums—raised problems for FDA, the agency responsible for regulating radiation-emitting devices such as lasers. What concerned FDA was that the so-called "entertainment lasers" might be used in unsafe ways and cause harm to consumers. If a medium- to high-power laser beam should strike a person's eye, for example, it could damage vision or even cause blindness. Prolonged exposure to high-power laser illumination can cause skin burns. Because of these dangers, FDA established safety standards for laser light shows. A company putting on such a show can deviate from the standards only if an "approved variance" is obtained from the Bureau of Radiological Health. The bureau grants such variances only if other precautions have been taken to assure safety.

Audience scanning, in which the laser beam actually sweeps through spectators, is a deviation from the standards for laser light shows. So, when the Bureau of Radiological Health learned that Laser Physics was using such scanning in its Soho show, one of the staff checked into the variance status of the company. Laser Physics had a variance but it included a provision that no audience scanning would begin until FDA had evaluated the safety controls. This had not been done. The bureau then asked that the agency's New York district investigate to see if Laser Physics was violating any other standards.

A New York investigator went unannounced to the show. He noted with more than just casual interest that the laser beam frequently passed quite close to the front row of spectators, dancing scarcely six feet above the floor; under standards for laser light shows, the laser beams must be kept at least three meters (about 10 feet) above the floor where the audience is seated.

After the show, the investigator presented himself to the management and showed his credentials and a notice of inspection. Then he checked out the equipment and noted some additional violations: mirrors used to reflect the laser beams did not have proper scanning safeguards to prevent exposure of the audience to hazardous radiation levels. And there was no safety mechanism to automatically terminate the beam if anyone from the audience stepped forward from the seating area into the area where radiation was hazardous.

The investigator told the company that the show was unsafe and that it was violating radiation safety standards. So it couldn't have come as much of a surprise to Laser Physics when it received a notice from the Bureau of Radiological Health a little later saying that the variance for the laser show was rescinded. Laser Physics is prohibited from producing other shows until the company obtains a new variance.

—Carol Ballentine is a member of FDA's public affairs staff.

Label Unmasked

Use of masking tape and felt-tipped pens are not satisfactory for relabeling a food product, a Pomeroy, Ohio, firm has discovered. Excelsior Salt Works agreed to recall approximately 400 pounds of relabeled salt because consumers were confused about the product's identity.

The company repacks salt products such as rock salt for de-icing and canning salt. Employees repacking 10-pound bags of canning salt from 80-pound bags ran out of bags with printed labels, so they "borrowed" from the stock of bags labeled for rock salt, covered the label with masking tape, and hand-lettered "Canning Salt" on the tape with a felt-tipped pen. Unfortunately, the original label was still visible through the tape. As the hand lettering became fainter with age, the original label became easier to read.

The problem came to light when a consumer called the **West Virginia Health Department** to complain that the product purchased as canning salt appeared to be rock salt. The company told the department that the salt was, in fact, canning salt but agreed to recall it to prevent further confusion. FDA's **Cincinnati District** monitored the recall.

Overcoming Reluctance

Products that emit radiation, such as X-ray equipment and microwave ovens, must meet certain safety and performance standards set by FDA's Bureau of Radiological Health before they can be marketed. Companies must affix labels to their products, certifying that they conform to the standards. That certification is based on a test prescribed by the standard or by a test program approved by BRH.

Bucky X-Ray International, a New York designer and distributor of X-ray equipment, failed to follow the requirements when it recently introduced a new cabinet X-ray system. When advertising for the unit came to the attention of BRH officials, the firm was reminded that it had not submitted the required report for a new cabinet X-ray and that the testing program had not been approved. Bucky replied that it was only advertising, not making or distributing the units.

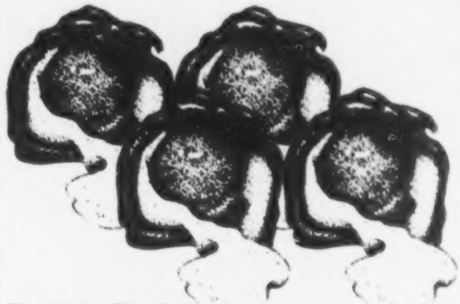
But even as it was saying this, Bucky had shipped an unassembled unit to a firm in Hartford, Conn. The Hartford firm complained to FDA's **Hartford Resident Post** that the unit would not operate properly, not knowing that a good deal more was amiss. FDA found that the unit at Hartford was not certified; did not meet the standard for cabinet X-ray systems; had improperly placed or was lacking warning labels; and did not have the required light to show when the unit is operating.

Meanwhile an FDA investigator, checking at Bucky's New York City office, discovered that another unit had been shipped to Chicago. Inspection of the unit by FDA's Chicago staff showed the same types of deficiencies.

FDA next went to Ban-Ray Products in Brooklyn, the actual manufacturer of the Bucky cabinets. There investigators found that four cabinets had been made but only two had been shipped. Then back to Bucky International in New York City to see if corrections were planned for the two units already shipped and in use. Bucky's management people refused to speak to the FDA investigator.

At this point, because Bucky would not cooperate and because the violative equipment had not been withdrawn from use, FDA decided to move against the firm.

The agency sent a recommendation to the U.S. attorney for the Southern District of New York seeking an injunction and civil penalty against the firm. Faced with these consequences, Bucky International and its president, Peter Bucky, agreed to a stipulation requiring repair of units already shipped to bring them into compliance with the standards, and withholding of shipment of X-ray equipment that fails to conform to the standards. Bucky was also found liable for $1,500 in civil penalties for its violations.



Back in Business

Rogers Candy Co. of Seattle, Wash., is back in business after being shut down a month for a complete housecleaning.

It's the second time in less than two years that Rogers has gone through the exercise. This time the action was backed by a court order obtained by FDA's **Seattle District** office.

Rogers is one of the principal producers of chocolates in the Pacific Northwest. The company has long had problems with sanitation. Rogers has had, in FDA parlance, "an active insect and rodent infestation" it seemed unable to correct.

Inspections by FDA and state of Washington officials in late 1979 revealed that candy was being produced and raw materials stored under insanitary conditions. A cleanup was attempted by the company. Inspections three months later showed some of the same problems, including rodent infestation in the equipment used to coat and cool the candy products. Rogers shut down long enough to fumigate and clean up the plant. But an April 1981 check found the equipment still infested.

At this point FDA filed a complaint for injunction with the U.S. district court in Seattle, asking that the plant cease operations until it was brought into compliance with the laws and regulations.

Company officials signed a consent decree, the plant was thoroughly cleaned and sealed against rodents and insects, and a sanitation control program adopted, with a sanitation expert hired temporarily. When FDA again inspected the plant and found it in compliance, Rogers resumed operation.

A Saucy Tale

Although FDA has experts in food sanitation, the agency almost never does actual restaurant inspections. These are the responsibility of city and county health departments, whose inspectors have long checklists concerning time and temperature of dish washing cycles, cleanliness of food storage areas, and other specifics of food service operation.

FDA does instruct these local inspectors, using workshops and other training aids. The agency also has prepared a widely used manual on food sanitation and has developed a model ordinance (set of regulations) that many states and localities have adopted as their own. (See *For Your Dining Pleasure—A Model Ordinance*, FDA CONSUMER, February 1980.)

But occasionally FDA gets an invitation to do a restaurant inspection that it cannot refuse. These are usually from U.S. Department of State officials arranging a dinner for a visiting chief of state, or from the presidential detail of the U.S. Secret Service.

One such request came earlier this year from the Secret Service. President Reagan was to be the guest of honor at an after-theater dinner at Le Cirque restaurant in New York City. FDA was asked to check out the restaurant's methods of food storage and preparation prior to the president's visit.

Food specialist Donald Green from FDA's **Region II New York** office did an afternoon inspection of Le Cirque several hours before the dinner was to be held. He looked through the kitchen and serving areas, checked the walk-in and reach-in refrigerators, and found things generally in order. He rated the restaurant "acceptable."

But he did not care for the slow cool-down of butter sauces (gravies) in a water bath. He asked that it be done in shallower pans, to allow for faster cooling so that bacteria would not have a chance to develop. Le Cirque chef Alain Sailhac objected, saying that sauces by tradition must be cooled slowly, to retain their flavor.

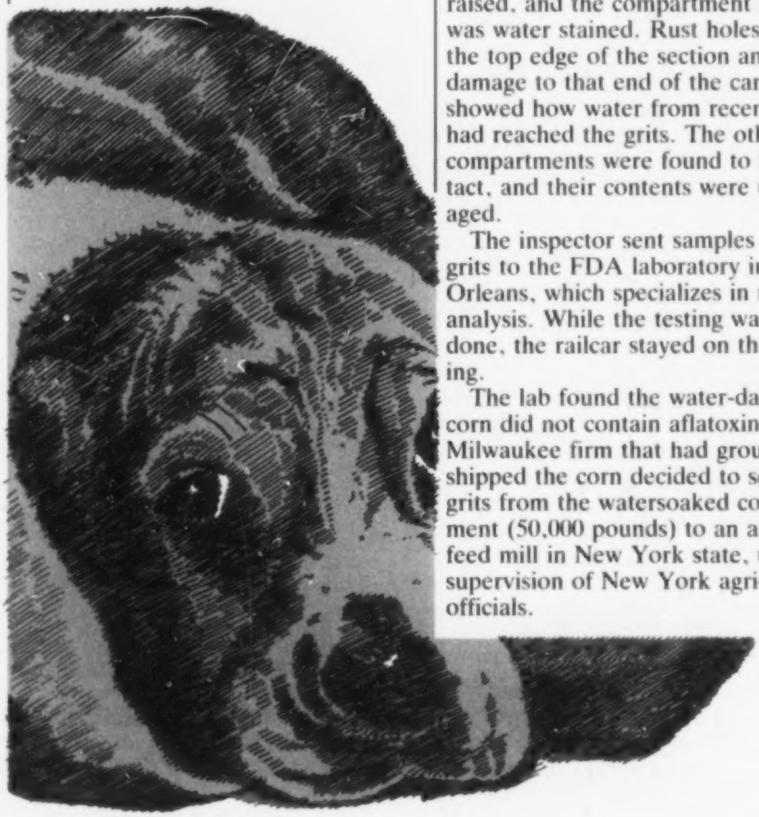
In this instance tradition yielded, because it was for the President. The sauces were cooled (quickly) and served with a menu that included giant Spanish scampi, scallops, duck, veal and other dishes.

4-D Meat

An FDA investigator recently discovered that a Libertyville, Ill., manufacturer was selling animal food that wasn't fit for a dog.

FDA's **Waukegan Resident Post** investigator was making an inspection of the Pine Tree Dog Food Co. when he noticed the firm was shipping frozen, raw meat in plastic casings. After a brief discussion with the owner, he learned that the meat came from dead, dying, diseased or disabled animals—what FDA refers to as 4-D meat.

The agency does not object to the use of 4-D meat in animal food as long as it has been properly processed to render it safe. The two processes commonly used are canning and rendering, but the investigator found no evidence that the company had used either process.



Since the products were unprocessed and because the firm had been selling them to kennels and pet owners, the meats, valued at $1,300, were subsequently seized by U.S. marshals.

True Grits

An FDA inspector from the **Buffalo District** office, doing a routine inspection of a brewery in Rochester, N.Y., was told by the brewmaster that some corn grits just received in a railroad hopper car had been rejected because of water damage.

To the inspector, water damage meant the possibility of mold growing on that corn. If the mold were *Aspergillus flavus* or *Aspergillus parasiticus*, a byproduct (aflatoxin) could form that would be hazardous to human health if the corn were eaten. He asked to see the railcar, which was still on the brewery siding.

The railcar was a three-section hopper, with hatches (covers) over each compartment. A strong musty odor came up from the grits when the hatch over the first section was raised, and the compartment itself was water stained. Rust holes along the top edge of the section and some damage to that end of the car showed how water from recent rains had reached the grits. The other two compartments were found to be intact, and their contents were undamaged.

The inspector sent samples of the grits to the FDA laboratory in New Orleans, which specializes in mold analysis. While the testing was being done, the railcar stayed on the siding.

The lab found the water-damaged corn did not contain aflatoxin, so the Milwaukee firm that had ground and shipped the corn decided to sell the grits from the watersoaked compartment (50,000 pounds) to an animal feed mill in New York state, under supervision of New York agricultural officials.

Long Trip, Light Baggage

While checking out consumer complaints about the quality of some canned shrimp, FDA's **Seattle District** found that the shrimp may have done more traveling than a lot of people do. Some information is still shrouded in mystery, but the district did piece together a lengthy itinerary.

The shrimp originally had been canned in India and shipped to the United States in 1974. The shipment was refused entry by FDA, probably at the Port of New York, and was then exported to England. In 1979 part of the shipment was again shipped to the United States and was purchased by the New England Fish Co., Seattle, Wash. That company recanned the shrimp and distributed it, and 74 cases ended up in a food store in Yakima, Wash. The store manager contacted Seattle district's Yakima Resident Post after two customers complained that the shrimp was of inferior quality.

The Seattle lab analyzed samples, confirmed that the product was of poor quality, and also found that the cans were short weight and below the standard for fill of container. Because of the economic and labeling violations, approximately 1,152 cans of the shrimp, valued at $1,200, were subsequently seized by the U.S. marshal.

Shell Games

Earlier this year the **Rhode Island Department of Health,** working with the **Connecticut health department,** seized 113 bags of oysters valued at $1,880 being offered for sale by two dealers. The oysters had not been certified by the state as coming from waters safe for shellfishing. They were not certified because they had been taken illegally from a contaminated oyster bed off the Connecticut coast.

The dealers lost the oysters, but the public gained. The oysters, still alive, were transported to an approved, clean-water location in Rhode Island. There, over the weeks, they would pump the clean water through their systems, rid themselves of the contaminants, and then be available for public harvesting.

The operators of a company on Long Island tried a similar maneuver, taking clams from an area closed to shellfishing. Unknown to them, they were being watched by New York State conservation officers.

Using a hydraulic dredge boat, employees of the Freeport Clam Co. of Long Island took 300 bushels of surf clams from condemned (contaminated) ocean waters off Rockaway Beach. Back in port, the operators loaded the clams into a trailer truck, then left the truck overnight at the driver's home.

The next morning the driver hauled the clams to a packing plant 80 miles away to be processed for human food. The load was seized at the plant by officers who had followed the entire operation, from the dredging to waiting overnight near the driver's home to trailing him on the trip to the packer. The contaminated clams were destroyed by burial in a landfill, and the Freeport firm was charged.

Actually the company did itself in. Freeport had a permit to take clams from the closed waters, but the clams were to be used only as bait for fish, not for human food. Had Freeport waited a few weeks, the New York City sewage dumped into the waters would have been routinely treated with chlorine. When the water is thus treated, clams can be harvested for food throughout the summer months.

Exit Not Laughing

A patient at Methodist Hospital in Brooklyn was understandably distressed when he noticed that the tank in his room, supposedly filled with medical oxygen, was labeled nitrous oxide. If the tank held nitrous oxide (laughing gas), he was in trouble, because he'd already breathed some of the tank's contents.

But it was Liquid Carbonic, the company that supplied the gas, who was in trouble, and by the time the confusion was sorted out, the company's Brooklyn operation was closed.

Medical gasses are packed in color-coded tanks that are familiar to hospital personnel. Oxygen is green, nitrogen yellow. The five-foot tanks have stick-on labels that tell what gas is inside. What the label says should match the color of the tank. Oxygen and nitrogen tanks also have different couplings. There are hose couplings to match, so it should be difficult to make a wrong connection. A wrong connection could be disastrous, because oxygen is flammable and needs special handling.

Luckily the error was only in the labeling. An FDA investigation showed that Liquid Carbonic kept its oxygen and nitrogen labels in the same stack in its Brooklyn facility. Oxygen tanks were filled on the premises, and nitrogen tanks came over pre-filled from New Jersey. If pre-filled tanks had damaged labels, a new label was supposed to be attached. Apparently the wrong one was used in this instance. Hospital staff had not looked closely at the label because they knew the green color of the tank meant it held oxygen.

The firm earlier had been warned by FDA's **New York District** office of this kind of mixup, and company officials in Chicago had promised better control.

On the same day that Methodist Hospital had called the agency about the wrong label, a complaint had come in to FDA from an anesthesiologist in another Brooklyn hospital, wondering why his oxygen tank was labeled nitrogen. Again the supplier was Liquid Carbonic.

Faced with these multiplying problems, the company recalled the medical gasses it had distributed from its Brooklyn plant and closed that facility for good.

—Compiled and written by Carol Ballentine, Michael Herndon and Richard Thompson

Postal Service Cases

Complaints Filed by Law Department Under 39 U.S.C. 3005 (False Representation)

March 20, 1981: **Mohr Cosmetics, Ltd.**, 16218 Ventura Blvd., #9, Encino, California. Advertising and sale through the mail of the product "Firmacel," representing the ability to "restore firmness and eliminate lines around the nose, mouth and eyes."

March 20, 1981: **Cosvetic Labs,** P.O. Box 49087, Atlanta, Georgia. Advertising and sale through the mail of the product "Cellular Formula 0-47A." The published advertisement states in part, "Cellular Formula 0-47A can provide enzymes and growth factors essential to development stages which enhance metabolism and subsequently rejuvenation. That means an improvement that's more than cosmetic. It means younger-looking skin."

March 20, 1981: **Cosvetic Labs,** P.O. Box 49303, Atlanta, Georgia. Advertising and sale through the mail of the product "Cellular Formula 0-47B." The ad states in part, "it is designed to rejuvenate aging skin and keep young skin looking that way."

March 20, 1981: **The New Body Boutique,** 37 Eleventh Avenue, Huntington Station, New York. Advertising and sale through the mail of the product "Second Skin—The Space Age Slenderizer," representing the ability to "lose up to 5 pounds in 15 minutes—5 inches in 5 hours! Lose pounds and inches from waist, hips, and thighs, now! Shed unwanted weight and excess flab in just minutes."

March 20, 1981: **Quest Research, Inc.**, P.O. Box 20499, Atlanta, Georgia. Advertising and sale through the mail of the product "Skin Deep," representing the ability to "have clear skin in only 5 days. Everyone is familiar with the heartbreak of acne skin blemishes. If you suffer from this common problem or know someone else who does, now there is a fast working, long lasting solution . . . the real secret behind Skin Deep is that it acts as a shield against further acne development."

March 27, 1981: **California Medical Research,** P.O. Box 4855, San Diego, California. Advertising and sale through the mail of the product "Selenium Plus 2." The ad states in part, "a glowing, firmer skin, healthier hair, stronger nails, increased energy and vigor and so much more . . . RNA is helping to improve muscle strength, vitality and cellular reproduction."

March 27, 1981: **Bio-Vim Laboratories,** 4099 Tamiami Trail North, Suite 311, Naples, Florida. Advertising and sale through the mail of the product "Prostazinc," representing the ability to relieve prostate problems.

March 31, 1981: **House of Grayson,** 330 S. Mentor, Suite 310, Pasadena, California. Advertising and sale through the mail of the product "Mr. Arthur," representing the ability to relieve arthritis.

April 21, 1981: **Dr's Capsule Plan,** 1255 Post Street, San Francisco, California. Advertising and sale through the mail of the product "Dr's Capsules," representing the ability to reduce weight loss.

April 21, 1981: **Jojoba Industries,** P.O. Box 7212, Phoenix, Arizona. Advertising and sale through the mail of the product "Jojoba Joy," representing the ability to cure various skin disorders.

April 21, 1981: **Standard Research Labs,** P.O. Box 852, Pompano Beach, Florida. Advertising and sale through the mail of the product "ENZ-3 System," representing the ability to cause enlargement of breast tissues.

April 21, 1981: **Quest Research,** P.O. Box 49024, Atlanta, Georgia. Advertising and sale through the mail of the product "Athlete's Vitamin." The ad states in part, "provides an active individual with an easy, convenient method to increase the efficiency of oxygen utilization. Use the vitamin serious athletes use."

April 21, 1981: **Earthquest, Ltd.,** P.O. Box 49087, Atlanta, Georgia. Advertising and sale through the mail of the product "Improved Right Places," representing the ability to increase the bustline.

April 21, 1981: **Cosvetics,** P.O. Box 53098, Atlanta, Georgia. Advertising and sale through the mail of the product "BEZ-P39," representing the ability "to deliver up to a 10% increase in the size of your bust."

April 21, 1981: **Cosvetic Labs, Inc.,** P.O. Box 1097, Deerfield Beach, Florida. Advertising and sale through the mail of the product "Your Image," representing the ability to "increase your bustline."

May 1, 1981: **Cosvetic Labs,** P.O. Box 49087, Atlanta, Georgia. Advertising and sale through the mail of the products "Vitagland-F and Vitagland-M," representing the ability "to maintain youthful appearance."

May 13, 1981: **Inter-Bay Distributing,** P.O. Box 1786, Pinellas Park, Florida. Advertising and sale through the mail of "Stimulants." These stimulants are being sold as "look-alike" narcotics.

May 13, 1981: **R.S.L. Pharmacal, Inc.,** 106 North Main Street, Bel Air, Maryland. Advertising and sale through the mail of "Stimulants." These stimulants are being sold as "look-alike" narcotics. The published advertisement states in part, "why pay more from an unlicensed street dealer? Stimulants, legal, very effective, and profitable. Satisfaction guaranteed."

May 13, 1981: **J&L Pharmaceutical Distributing,** P.O. Box 953, Sandusky, Ohio. Advertising and sale through the mail of "Stimulants." These stimulants are being sold as "look-alike" narcotics. The ad states in part, "made to look and act like the real prescription drugs that only doctors can prescribe. The pills are safe and quick acting."

May 13, 1981: **The Source,** 1706 Central SE., Albuquerque, New Mexico. Advertising and sale through the mail of "Stimulants." These stimulants are being sold as "look-alike" narcotics. The ad states in part, "like stimulation? Look inside. Legal stimulants at wholesale prices. No legal stimulants stronger than some prescription drugs pick-you-up and stimulate you."

May 13, 1981: **GC Distributing,** P.O. Box 3068, Elmira, New York. Advertising and sale through the mail of "Stimulants." These stimulants are being sold as "look-alike" narcotics.

May 14, 1981: **Speciality Sales Company,** 130 Buena Vista Avenue, Yonkers, New York. Advertising and sale through the mail of the product "Sauna—Slimmer," representing the ability to reduce weight.

May 14, 1981: **H & L Labs, Inc.,** 18 Lois Street, Norwalk, Connecticut. Advertising and sale through the mail of the product "Quadplan," representing the ability to cause weight loss.

May 14, 1981: **The Diet House, Inc.,** 95 M South Hoffman Lane, Central Islip, New York. Advertising and sale through the mail of the product "Guarana," representing the ability to cause weight loss.

May 18, 1981: **That Special Look, Inc.,** P.O. Box 1490, Pompano Beach, Florida. Advertising and sale through the mail of the product "Slim Away," representing the ability to cause weight loss.

May 19, 1981: **Leucadia Pharmacals,** 103 N. Highway 101, Leucadia, California. Advertising and sale through the mail of the product "Prost-Rite Tablets," representing the ability to relieve "the most common prostate trouble."

May 27, 1981: **The New Body Boutique,** 2105 Lakeland Avenue, Ronkonkoma, New York. Advertising and sale through the mail of the product "Shrink—Wrap System," representing the ability to "melt inches away."

June 2, 1981: **Nutritional Life Corporation,** 535 Fifth Avenue, New York, New York. Advertising and sale through the mail of the product "ZN Mega Mineral Tea," representing the ability "to repair and rebuild the prostate. To give it new health and power. To renew potency and vitality! And to do it in just 4 to 8 weeks—naturally—without surgery!"

June 5, 1981: **C-T Enterprises,** P.O. Box 6465, Glendale, California. Advertising and sale through the mail of the product "Super Shaper." The ad states in part, "melt away inches without dieting! Super shaper works on a scientific principle that uses body heat to melt away unwanted inches and pounds."

June 8, 1981: **Athena Products, Ltd.,** P.O. Box 14152, Atlanta, Georgia. Advertising and sale through the mail of the product "Super RNA Complex." The ad states in part, "RNA stands out as the most thoroughly proven and effective of all the nutritional anti-aging therapies."

June 9, 1981: **Orgone Energy Workshop,** Box 189, Walnut, Berkeley, California. Advertising and sale through the mail of the product "Orgone Energy Blanket," representing the ability "to absorb healing life energy directly from atmosphere."

June 11, 1981: **Phun Pharmaceuticals,** P.O. Box 2118, Gaithersburg, Maryland. Advertising and sale through the mail of "Stimulants." These stimulants are being sold as "look-alike" narcotics.

June 11, 1981: **Midsouth Pharmaceuticals,** P.O. Box 584 Hixson, Texas. Advertising and sale through the mail of "Stimulants." These stimulants are being sold as "look-alike" narcotics.

June 11, 1981: **Capricorn Pharmaceuticals,** Box 15393, Chattanooga, Tennessee. Advertising and sale through the mail of "Stimulants." These stimulants are being sold as "look-alike" narcotics.

June 11, 1981: **C & C Vitamins & Sundries, Inc.,** P.O. Box 455, Pittsburgh, Pennsylvania. Advertising and sale through the mail of "Stimulants." These stimulants are being sold as "look-alike" narcotics.

June 11, 1981: **Bob's Sundries, Inc.,** P.O. Box 7908, Pittsburgh, Pennsylvania. Advertising and sale through the mail of "Stimulants." These stimulants are being sold as "look-alike" narcotics.

June 11, 1981: **Don's Sundries,** 400 Nehrig Drive, Indiana, Pennsylvania. Advertising and sale through the mail of "Stimulants." These stimulants are being sold as "look-alike" narcotics.

June 16, 1981: **Rel-Eeze Distributors,** P.O. Box 247, Worth, Illinois. Advertising and sale through the mail of the product "Rel-Eeze," representing the ability "to give you the relief from pain you want in a matter of minutes . . . it is helping thousands of sufferers from arthritis, rheumatism, bursitis, and lumbago."

June 16, 1981: **Nutrition Headquarters,** 104 W. Jackson Street, Carbondale, Illinois. Advertising and sale through the mail of the product "Rel-Eeze," representing the ability "to give you the relief from pain you want in a matter of minutes . . . it is helping thousands of sufferers from arthritis."

June 25, 1981: **Easy-Off Slimmer,** 7 First National Plaza, Canton, Ohio. Advertising and sale through the mail of the product "Easy-Off Waist Slimmer." The ad states in part, "guarantees you can lose 4-8 inches from your waist and tummy the first 24 hours . . . As soon as you slip it on, the Slimmer starts to concentrate your body's natural heating effect."

False Representation Orders Issued by Judicial Officer Under 39 U.S.C. 3005

April 24, 1981: Against **Relief,** P.O. Box 23181, Washington, D.C. Satisfactory evidence was presented to the Postal Service that Relief and their representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Prostabs." The ad states in part, "what would you give if you might get rid of prostate misery—FAST—with no risk on your part—and do it for pennies a day. Just think what it would be like with your problems gone."

April 28, 1981: Against **House of Grayson,** 330 S. Mentor, Suite 310, Pasadena, California. Satisfactory evidence was presented to the Postal Service that House of Grayson and their agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Mr. Arthur," representing the ability to relieve arthritis.

April 30, 1981: Against **Bio-Vim Laboratories,** 4099 Tamiami Trail North, Suite 311, Naples, Florida. Satisfactory evidence was presented to the Postal Service that Bio-Vim Laboratories and their representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Prostazinc." The ad states in part, "New hope for men with prostate or bladder problems. If you're experiencing more frequent, painful, or delayed urination, or the feeling that your bladder is always full, ask your doctor about supplementing your diet deficiency with zinc."

May 7, 1981: Against **Nature Life Products Inc.,** 95 M South Hoffman, Central Islip, New York. Satisfactory evidence was presented to the Postal Service that Nature Life Products Inc. and their agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "RNA + 13 No Aging Diet," representing the ability "to take years off your appearance . . . not just pounds off your figure that programs rich in nucleic acid may help reduce breathlessness and fatigue! Combat many skin disorders."

May 7, 1981: Against **Natures Harvest Inc.,** 95 M South Hoffman Lane, Central Islip, New York. Satisfactory evidence was presented to the Postal Service that Natures Harvest Inc. and their representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising "RNA + Plus." The ad states in part, "the foundation of the 'no aging' diet concept is nucleic acid . . . our bodies already have nucleic acid, but some doctors feel that we need more to stay healthy than our bodies can manufacture. . . . here's the fabulous breakthrough news: doctors have discovered that it is possible to synthesize nucleic acid from food . . . a radically new approach to health and nutrition that's the secret of the famous 'no aging' diet."

May 15, 1981: Against **H-E-L-P,** 2310 Central Avenue, Memphis, Tennessee. Satisfactory evidence was presented to the Postal Service that H-E-L-P and their agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Potency Plus," representing the ability to "have a positive effect on such troubles as bad eyesight, hearing problems, constipation, male problems, nerve ailments, headaches, hayfever, arthritis, skin problems and sexual inadequacies."

May 21, 1981: Against **Diet Products Inc.,** 1 West Main Street, Smithtown, New York. Satisfactory evidence was presented to the Postal Service that Diet Products Inc., and their representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising "Anfamine." The ad states in part, "you grow slimmer and slimmer from meal to meal . . . and stay slim for the rest of your life."

May 22, 1981: Against **Dr's Capsule Plan,** 1255 Post Street, San Francisco, California. Satisfactory evidence was presented to the Postal Service that Dr's Capsule Plan and their agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Dr's Capsules," representing the ability to "lose the fat forever. Lose 10, 20, 30 . . . even 60 pounds or more—without time consuming exercise—without one moment of hunger!"

May 22, 1981: Against **Jojoba Industries,** P.O. Box 7212, Phoenix, Arizona. Satisfactory evidence was presented to the Postal Service that Jojoba Industries and their representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising "Jojoba Joy." The ad states in part, "ancient Indian remedy for seborrhea, psoriasis, acne, dry skin, scalp and hair."

June 4, 1981: Against **Natures Harvest,** 95 M South Hoffman Lane, Central Islip, New York. Satisfactory evidence was presented to the Postal Service that Natures Harvest and their agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Bio-Grow Hair Renewal Gel." The ad states in part, "why be bald? Now . . . at last . . . actually grow hair! . . . fabulous scientific breakthrough! Reduces fallout, fights male pattern baldness!"

June 25, 1981: Against **Inter-Bay Distributing Company,** P.O. Box 1786, Pinellas Park, Florida. Satisfactory evidence was presented to the Postal Service that Inter-Bay Distributing and their representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising "Stimulants." These stimulants are being sold as "look-alike" narcotics.

June 26, 1981: Against **Athena Products Ltd.,** 3176 Marjan Drive, Atlanta, Georgia. Satisfactory evidence was presented to the Postal Service that Athena Products and their agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "New Start Natural Hair Vitamins," representing the ability to prevent hair loss and reversing baldness.

June 30, 1981: Against **Contemporary Mission Inc.,** 285 A Saugatuck Avenue, Westport, Connecticut. Satisfactory evidence was presented to the Postal Service that Contemporary Mission Inc. and their representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Guaranteed Relaxation Diet Plan." The ad states in part, "lose weight even while you sleep! We guarantee the relaxation diet can free you of 5, 10, 15, 20 pounds or more of unwanted flab and fat."

Notices of Judgment

NOTICES OF JUDGMENT on Seizure Actions

FOOD/Poisonous and Deleterious Substances

Cornmeal, at Chipley, N. Dist. Fla.

Charged 2-3-81: when shipped by Dixie Lily (Div. Martha White Foods, Inc.), Tifton, Ga., the article contained the added poisonous and deleterious substance aflatoxin; 402(a)(1). Default decree ordered destruction. (F.D.C. No. 63309; S. Nos. 81-268-381/3; N.J. No. 1)

FOOD/Contamination, Spoilage, Insanitary Handling

Cranberry sauce, jellied, canned, at Tonawanda, W. Dist. N.Y.

Charged 6-9-81: while held for sale, the article was contained in rusted and leaking cans; 402(a) (3). Default decree ordered destruction. (F.D.C. No. 63486; S. No. 81-256-056 et al.; N.J. No. 2)

Fig paste, and **fig-square filling mix,** at Lynn, Dist. Mass.

Charged 3-13-81: when the fig paste was shipped by Bodegas Jose M. Sogas, Barcelona, Spain, the article contained mites; and while the fig-square filling mix was held for sale after manufacture locally from fig paste, the article had been prepared under insanitary conditions; 402(a) (3) and (4). Consent decree authorized release to Buy Rite Co., Lynn, Mass., for salvaging. (F.D.C. No. 63347; S. Nos. 81-155-933, and 81-230-354; N.J. No. 3)

Flour, at Nanuet, S. Dist. N.Y.

Charged 10-9-80: while held by Silverock Baking Corp., Nanuet, N.Y., the article had been held under insanitary conditions; 402(a)(4). Default decree ordered destruction. (F.D.C. No. 63141; S. No. 80-138-076; N.J. No. 4)

Flour, at Rochester, W. Dist. N.Y.

Charged 5-1-81: while held by Petrillo Bros. Bakery, Inc., Rochester, N.Y., the article had been held under insanitary conditions; 402 (a)(4). Default decree ordered destruction. (F.D.C. No. 63465; S. No. 81-256-147; N.J. No. 5)

Orange segments (broken), Mandarin, canned, at Miami, S. Dist. Fla.

Charged 2-11-81: while held for sale, the article was contained in swollen and leaking cans; 402(a)(3). Decree ordered destruction. (F.D.C. No. 63325; S. No. 81-239-403; N.J. No. 6)

Rice, at Philadelphia, E. Dist. Pa.

Charged 6-22-81: while held by Beautiful Foods, Inc., Philadelphia, Pa., the article had been held under insanitary conditions; 402(a)(4). Default decree ordered destruction. (F.D.C. No. 63467; S. No. 81-230-444; N.J. No. 7)

Rice, and **other foodstocks,** at Miami, S. Dist. Fla.

Charged 3-5-81: while held by J. Garcia Distributors of Florida, Inc., Miami, Fla., the articles had been held under insanitary conditions; 402(a)(4). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63389; S. No. 81-239-658; N.J. No. 8)

Rice flour, at San Francisco, N. Dist. Calif.

Charged 3-28-77: while held by Wing Sing Chong Co., Inc., San Francisco, Calif., the article contained rodent filth and had been held under insanitary conditions; 402(a)(3) and (4). Default decree ordered destruction. (F.D.C. No. 61130; S. No. 77-49-117; N.J. No. 9)

Tomato paste, canned, at Wilmington, Dist. Del.

Charged 11-21-80: while held for sale, the article was contained in swollen cans and the article's can linings were deteriorating; 402(a)(3). Consent decree ordered destruction. (F.D.C. No. 63122; S. No. 80-224-961; N.J. No. 10)

DRUGS/Human Use

Chlorthalidone tablets, hydroxyzine HCl tablets, hydroxyzine pamoate capsules, furosemide tablets, prochlorperazine capsules, and **chlorothiazide with reserpine tablets,** at Philadelphia, E. Dist. Pa.

Charged 3-6-80: when shipped by Pharmadyne Laboratories, Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The shipper claimed the articles. Pursuant to stipulation, the action was transferred to the District of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62825; S. No. 80-208-585; N.J. No. 11)

Chlorthalidone tablets, hydroxyzine HCl tablets, allopurinol tablets, chlorothiazide with reserpine tablets, diethylpropion HCl tablets, furosemide tablets, hydroxyzine pamoate capsules, and **trimethoprim with sulfamethoxazole tablets,** at Auburn Heights, E. Dist. Mich.

Charged 3-6-80: when shipped by Pharmadyne Laboratories, Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper who denied the charge. Pursuant to stipulation, the action was consolidated with four similar Michigan actions, and transferred to the District of New Jersey for consolidation for trial with another similar action. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62793; S. No. 80-208-557; N.J. No. 12)

Disodium edetate injection from two manufacturers, two seizure actions, at Belle Chasse, E. Dist. La.

Charged 6-10-75 and 11-5-75, and amended 5-20-76 to request injunctive relief (see N.J. No. 24 of this issue of FDA CONSUMER): while held by Meadowbrook Hospital, Belle Chasse, La., who intended the articles for use for generalized arteriosclerosis and other disease conditions, the articles lacked adequate directions for use for such uses and were not exempted therefrom because the articles lacked adequate information for the articles' use; 502(f)(1).

The articles were claimed by H. Ray Evers, M.D., owner and operator of Meadowbrook Hospital, Belle Chasse, La. The claimant moved for a temporary restraining order and a preliminary injunction against the government enjoining any interference with the claimant's use, custody and control of the articles. The motion by the claimant for a temporary restraining order against the government was denied. The claimant moved to dismiss the action and subsequently moved to convert such motion into a motion for summary judgment. The court authorized such conversion into a motion for summary judgment. However, the court denied the claimant such summary judgment.

The claimant served written interrogatories on the government. The government objected to the interrogatories and the claimant moved to compel answers to the interrogatories. After argument before the court, the court denied the claimant's motion as to two interrogatories but ordered the government to answer the other interrogatories with certain restrictions as stated by the court. After the government amended its complaint to include injunctive relief, the action was tried by the court. The court granted an injunction, saying:

". . . This suit was originally instituted as a forfeiture action for the seizure and condemnation of the drug Disodium Edetate (EDTA), which is held for sale at Meadowbrook Hospital, on the ground that the drug was misbranded after shipment in interstate commerce.

"By way of amended complaint, the United States sought a preliminary injunction. . . .

"Initially, this case began as an action for the seizure of EDTA, which was allegedly misbranded. However, as the prayer for injunctive relief indicates, the government is now not only attempting to enjoin the misbranding of EDTA, but also its administration. The issuance of the injunction will avoid the necessity of the government making multiple, and perhaps daily, seizures of EDTA in order to prevent the misbranding of EDTA.

MISBRANDING

"Initially, the government contends that the EDTA at Meadowbrook Hospital is misbranded within the meaning of 21 U.S.C. § 352(f)(1). On June 12, 1975, at an evidentiary hearing on Dr. Evers' motion to dismiss the Government's suit, this Court found: 'We have here an instance where a man is broadcasting to the public through other physicians a widespread use of a drug for which not only is the drug not labeled, but for which use is contraindicated. The Court finds the evidence indicates the drug is still in commerce and that under these circumstances, the actions of Dr. Evers, the claimant, have been shown to this Court's satisfaction, to constitute mislabeling or misbranding.' The evidence adduced at the injunction hearing discloses that EDTA has continued to be misbranded by Dr. Evers and his associates at Meadowbrook Hospital.

"The evidence is undisputed that the defendants have used EDTA in the treatment of arteriosclerosis and other circulatory diseases (chelation therapy). However, the labeling of disodium edetate is as follows:

DISODIUM EDETATE

WARNING (BOX)

"The use of this drug in any particular patient is recommended only when the severity of the clinical condition justifies the aggressive measures associated with this type of therapy.

ACTION

"Disodium edetate forms chelates with the cations of calcium and many divalent and trivalent metals. Because of its affinity for calcium, disodium edetate will produce a lowering of the serum calcium level during intravenous infusion. Slow infusion over a protracted period may cause mobilization of extracirculatory calcium stores. The chelate thus formed is excreted in the urine. Disodium edetate exerts a negative inotropic effect upon the heart. . . .

INDICATIONS

"Disodium edetate is indicated in selected patients for the emergency treatment of hypercalcemia and for the control of ventricular arrhythmias and heart block associated with digitalis toxicity. . . .

CONTRAINDICATIONS

"Disodium edetate is contraindicated in anuric patients. It is not indicated for the treatment of generalized arteriosclerosis associated with advancing age.

WARNING

"See box warning above.

"Rapid intravenous infusion or attainment of a high serum concentration of disodium edetate may cause a precipitous drop in the serum calcium level and may result in fatality. Toxicity appears to be dependent upon both total dosage and speed of administration. The rate of administration and dosage should not exceed that indicated in Dosage and Administration.

"As can clearly be seen, not only does the labeling fail to bear adequate direction for its use in the treatment of circulatory diseases, but also it is specifically contraindicated for that type of treatment.

"The phrase 'adequate directions for use' has been construed to mean directions which are readily intelligible to those without special training. *Alberty Food Products* v. *United States*, 194 F.2d 463 (9th Cir. 1952). Nonetheless, 21 U.S.C. § 352 (f)(1) recognizes that there are some drugs which, by virtue of their characteristics, such as toxicity or other potentiality for harm, cannot bear adequate directions for lay use. However, such drugs may be marketed if they comply with the applicable requirements of 21 C.F.R. § 201.100, including labeling which contains: '(d)(1) . . . adequate information for such use, including indications, effects, dosages, routes, methods, and frequency and duration of administration, and any relevant hazards, contraindications, side effects, and precautions, under which practitioners licensed by law to administer the drug can use the drug safely and for the purposes for which it is intended, including all purposes for which it is advertised or represented. . . .'

"Courts have held that the intended use of a drug is revealed by a number of factors associated with the actual use, promotion, advertising and sale of the drug. . . . Whether an article is intended to be used for a particular drug use has been determined from newspapers and magazine advertisements, store placards, and television . . . from letters and oral representations, . . . from speeches delivered at a public lecture hall, . . . from statements of an authorized distributor, . . . and from a radio broadcast. . . .

"Testimony at the injunction hearing established that Dr. Evers has held a press conference and distributed promotional literature advocating EDTA therapy for cardiovascular therapy, and that promotional literature of a same sort was distributed at a convention of the National Health Federation. It was shown that Dr. Evers continued to distribute chelation therapy advertising to prospective patients and both he and Meadowbrook Hospital enjoy a national reputation as employing EDTA in the treatment of arteriosclerosis.

"Accordingly, it is this Court's conclusion that the intended use of EDTA at Meadowbrook Hospital is in the treatment of arteriosclerosis and that the failure of the drug's label to comply with 21 C.F.R. § 200.100 causes it to be misbranded within the meaning of 21 U.S.C. § 352 (f)(1).

AVAILABILITY OF INJUNCTIVE RELIEF

"At the outset, the Court notes that the evidence presented as to the existence, *vel non*, of irreparable injury caused by the misbranding of EDTA was mixed. Nevertheless, the Court is convinced that unless the continued misbranding of EDTA at Meadowbrook Hospital is enjoined, serious and irreparable harm will occur to the individual patients at the hospital and the public generally. . . .

"Dr. Kenneth C. Schneider, who is a medical consultant at the Dallas Regional Office of the Public Health Service, testified in detail about three deaths he concluded were directly caused by the administration of EDTA at Meadowbrook Hospital. Dr. Schneider, who was qualified as an expert in preventive and public health medicine, further testified that five other patients died either from renal failure or congestive heart failure following administration of the drug.

"Dr. John David Spence, a qualified expert in internal medicine, clinical pharmacology and neurology, testified concerning his review of the medical histories of twenty-one Meadowbrook Hospital patients, fourteen of which he concluded died from EDTA therapy. Causes of death ranged from insulin shock, congestive heart failure caused by administration of a high saline solution carrying EDTA, and renal failure.

"Finally, Dr. George L. Bailey, Clinical Professor of Medicine at Tulane University Medical School, and an expert in toxicology and nephrology, testified that EDTA should be employed solely for the treatment of lead poisoning (and even then at great risk). One woman patient retained nearly forty pounds of edematous fluid because Meadowbrook Hospital maintained her on a highly saline solution containing EDTA, which fluid Dr. Bailey removed by means of dialysis.

"Admittedly, several doctors and a number of individuals testified on Dr. Evers' behalf as to the beneficial effects of EDTA chelation therapy. The Court in balancing the value of this testimony is satisfied that the possible benefits of the EDTA therapy employed at Meadowbrook is far outweighed by the serious actual and potential damage caused by the drug in such therapy. Unrebutted evidence has established that EDTA chelation therapy has been indiscriminately applied to patients at Meadowbrook Hospital and that a number of them have died as a result. This Court is not in a position to condone the haphazard application of a drug for treatment of conditions for which its use is contraindicated. To do so would be to authorize the deaths of many in the faint hope of saving a few.

"As a general proposition, the Food and Drug Administration is charged with the responsibility of removing misbranded drugs from the market. Normally, this is done by seizure of the article in question. 21 U.S.C. § 334. However, in the case at bar, the Government wishes to go one step further by enjoining the actual administration of EDTA by Dr. Evers and his employees at Meadowbrook Hospital. Initially, the Court expressed concern over the possibility that such an injunction would constitute an unwarranted interference with the practice of medicine. However, a closer analysis of the jurisprudence and the particular facts of this case reveal that the injunctive relief as requested by the Government is not only lawful but also compelled.

"In *United States* v. *Hoxsey Cancer Clinic*, 198 F.2d 273 (5th Cir. 1952), the Court authorized the issuance of an injunction against a cancer clinic staffed by licensed physicians from misbranding drugs dispensed to patients and physicians in interstate commerce. In sanctioning injunctive relief against the physicians employed at the clinic, the Court noted that it was its 'duty to adjudge the merits of the case in the light of the provisions of the Federal Food, Drug and Cosmetic Act, supra, which close the channels of interstate commerce against drugs which are misbranded.' . . .

"In the case at bar, the Court feels that the requested injunction is justified as the only possible means of removing the misbranded drugs from interstate commerce. The evidence has established that Dr. Evers and his employees at Meadowbrook Hospital have continued to obtain quantities of EDTA and applied it to uses for which it is mislabeled and contraindicated. By enjoining the administration of EDTA at Meadowbrook the Government will not have to resort to multiple, and perhaps daily, seizures of the drug. Furthermore, mere seizure of the drug, in this case, would be a particularly inefficient means of preventing the misbranding of EDTA. In view of Dr. Evers' demonstrated proclivity for administering the drug for treatment for which its use is contraindicated, irreparable harm may occur to patients before the drug could be seized.

"The Court is of the further opinion that such an injunction will not interfere with or regulate the practice of medicine in any degree greater than it is already regulated under the Food, Drug and Cosmetic Act. As noted above, the Food and Drug Administration is charged with the responsibility of removing misbranded drugs from the flow of interstate commerce. The injunction as prayed for by the Government is the only practical and equitable means of carrying out that responsibility in the case at bar.

"Accordingly, it is ordered that the motion of the United States of America for a preliminary injunction as prayed for in its amended complaint be, and hereby is, granted." (F.D.C. Nos. 60320 and 60531; S. Nos. 53-951 H and 76-37-723; N.J. No. 13)

Furosemide tablets, at Ferndale, E. Dist. Mich.

Charged 6-3-80: when shipped by Superpharm Corp., Central Islip, N.Y., the article was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (F.D.C. No. 63041; S. No. 80-185-997; N.J. No. 14)

Furosemide tablets, at Philadelphia, E. Dist. Pa.

Charged 3-6-80: when shipped by Pharmadyne Laboratories, Inc., Elmwood Park, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). The article was claimed by the shipper. Pursuant to stipulation, the action was transferred to the District of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the article destroyed. (F.D.C. No. 62834; S. No. 80-208-591; N.J. No. 15)

Hydroxyzine HCl tablets, at Philadelphia, E. Dist. Pa.

Charged 10-18-79: when shipped by Pharmadyne Laboratories, Inc., Hackensack, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). The article was claimed by the shipper. Pursuant to stipulation, the action was transferred to the District of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the article destroyed. (F.D.C. No. 62554; S. No. 79-230-613; N.J. No. 16)

Oxygen, U.S.P., at South Beloit, N. Dist. Ill.

Charged 9-15-80: while held by Blackhawk Gases & Supply Co., South Beloit, Ill., who was engaged in repacking medical oxygen, the labeling of the article lacked adequate direction for use and lacked adequate information for use by licensed practitioners—502(f)(1); and the article was not labeled as prescribed by the UNITED STATES PHARMACOPEIA, since there was no statement as to whether or not the article had been produced by air liquefaction process—502(g). Consent decree authorized release to the dealer for relabeling. (F.D.C. No. 63153; S. No. 80-248-648; N.J. No. 17)

DRUGS/Veterinary

Ultra-Mend phosphate, bone meal, & manganese sulfate pet supplement, Ultra-Glo alpha tocopheryl acetate solution for pets, and **Ultra-Scorbate bone meal, ascorbic acid and manganese sulfate pet supplement,** at Mountain View, N. Dist. Calif.

Charged 7-25-80: while held by Frank W. McHugh Associates, Inc., Mountain View, Calif., who manufactured the articles using interstate bone meal, ascorbic acid, manganese sulfate and alpha tocopheryl acetate, the articles were new animal drugs and no approval of New Animal Drug Applications were in effect with respect to their use and intended use; 501(a)(5).

The articles were claimed by the manufacturers who denied the charge. The claimant demanded trial by jury. The government served interrogatories on the claimant and served requests for admissions. A consent decree of condemnation authorized release to the manufacturer for bringing into compliance. Subsequently, the claimant no longer wished to undertake the procedures for reconditioning the articles, and, pursuant to stipulation, the articles were ordered destroyed. (F.D.C. No. 63121; Nos. 80-253-032/4; N.J. No. 18)

MEDICAL DEVICES

Mini Gym Body Exerciser rope and pulley devices, and **bulk rope and pulley devices,** at Pennsauken Dist., N.J.

Charged 9-28-77: while held by General Home Products, Inc., Pennsauken, N.J., who held the bulk devices for packaging into retail containers (e.g., boxes labeled "Torso Trimmer . . . General Home Products Corporation . . . Burlington, N.J." and boxes labeled "Wonder Body Exercises . . . General Home Products Corporation . . . Burlington, N.J"), the labeling of the Mini Gym Body Exerciser devices contained false and misleading claims for slimming, trimming and shaping the body with only minutes of simple refreshing exercise, and the labeling of the bulk devices contained similar false and misleading claims; and the articles lacked adequate warnings against unsafe uses, since vignettes (Torso Trimmer and Wonder Body Exerciser boxes) depicted a user lying on his stomach to do the exercise, when such exercise might be injurious to persons with back or spinal problems; 502(a), 502(f)(1). The articles were claimed by the dealer who denied the charges. Subsequently, a consent decree of condemnation authorized release to the dealer for bringing into compliance. (F.D.C. No. 61357; S. No. 77-97-439 et al.; N.J. No. 19)

X-ray system, Traceray IV, at Seattle, W. Dist. Wash.

Charged 10-16-79: the article, which had been manufactured by Western States Supply, Ltd., Pueblo, Colo., was dangerous to health when used as directed, because the article would emit radiation beyond the pre-set exposure time—502(j); the accompanying labeling was false and misleading in claiming compliance with the regulation's standards, and in claiming that the devices would deliver the radiation exposure stated in the instruction manual—502(a); and the article's quality fell below its purported quality—501(c). Consent decree authorized release to the possessor for reconditioning. (F.D.C. No. 62557; S. No.

79-212-742; N.J. No. 20)

X-ray systems, Traceray III, two seizure actions, at Pinetops, E. Dist. N.C., and Cherryville, W. Dist. N.C.

Charged 11-2-79 and 11-22-79: the articles, which had been manufactured by Western States Supply, Ltd., Pueblo, Colo., were dangerous to health when used as directed because the devices would emit radiation beyond the pre-set exposure time—502(j); the accompanying labeling was false and misleading in claiming compliance with the regulation's standards, and in claiming that the devices would deliver the radiation exposure stated in the instruction manual—502(a); and the articles' quality fell below their purported quality—501(c). Consent decrees authorized release to possessors for reconditioning. (F.D.C. Nos. 62479 and 62485; S. Nos. 79-100-199 and 79-162-920; N.J. No. 21)

NOTICE OF JUDGMENT on Civil Penalty Action

Yoshida Dental (U.S.A.) Corp., at Hawthorne, C. Dist. Calif.

Charged 10-4-79 in a complaint for civil penalties, as well as injunction (see N.J. No. of this issue of FDA CONSUMER): that a number of dental X-ray units were found to be deficient and/or defective as follows: four specified units had installed a rubber stopper to prevent crushing of the power supply cable and consequent unintentional X-ray emission caused thereby; two specified units had had corrections made by unauthorized individuals and the user's manual had not been revised; and five other specified units had not had the user's manual revised; 42 U.S.C. 263(j)(a)(1) and (2).

A consent decree ordered that the corporation pay $20,000 in civil penalties. (Inj. No. 911; S. No. 79-140-286 et al.; N.J. No. 22)

NOTICES OF JUDGMENT on Injunction Actions

H. Ray Evers, M.D., president, and **Meadowbrook Hospital,** Belle Chasse, E. Dist. La.

Charged 5-20-76 in a complaint for injunction (as an amendment to seizure actions reported in N.J. No. 13 of this issue of FDA CONSUMER): that the defendants prescribed, dispensed, and administered disodium edetate injection and calcium disodium edetate at Meadowbrook Hospital to patients with diabetes, congestive heart failure, impaired renal function, arteriosclerosis, atherosclerosis, arthritis and other conditions for which use of the drugs was not indicated on their labeling, thereby having caused, and continuing to cause, such patients to be exposed to the unwarranted risk of grave physical injury and death; that the defendants had the ability to secure sufficient quantities of such drugs, and other drugs with chelating properties, either directly or indirectly, from potentially thousands of sources other than manufacturers, including as sources wholesalers, jobbers, distributors and others; that the plaintiff believed that, unless restrained, the defendant would continue to secure, hold for sale, prescribe, dispense and administer such drugs or other chelating agents to the detriment of patients residing at Meadowbrook Hospital; 502(f)(1).

After trial by the court, the court enjoined the defendants from the complained of violations with respect to disodium edetate injection. Dr. H. Ray Evers and the hospital appealed and moved for a stay of the injunction pending the appeal. The stay was denied. The appeal was dismissed for want of prosecution caused by the failure of the appellants to file their brief. Subsequently, Dr. H. Ray Evers moved to reinstate the appeal and the court authorized the reinstatement of the appeal. Ultimately, however, Dr. Evers suggested to the court that he wished to dismiss his appeal without prejudice and that he would bear all applicable appellate costs, and he so moved. Accordingly, the appeal was dismissed. (F.D.C. Nos. 60320 and 60531; S. Nos. 53-951 H and 76-37-723; N.J. No. 23)

H. Ray Evers, M.D., t/a Ra-Mar clinic, Montgomery, M. Dist. Ala.

Charged 3-29-78 in a complaint for injunction: that the defendant was a practicing physician who promoted, prescribed, dispensed and administered edetate calcium disodium (calcium EDTA) injection, U.S.P., in the treatment of arteriosclerosis (i.e., hardening of the arteries) while the drug was held for sale after interstate shipment; that arteriosclerosis was not a condition for use of the drug indicated by its labeling; that the defendant caused patients being treated at Ra-Mar Clinic to be exposed to the unwarranted risk of grave physical injury or death; that the drug's labeling did not and could not bear adequate prescribing information for treating arteriosclerosis (the use intended by the defendant), because the drug was not approved for such treatment and, accordingly, the drug's labeling lacked adequate directions for use and was not exempted as a prescription drug since its labeling lacked the required adequate information for use by licensed practitioners; that the defendant violated the law by promoting the use of the drug and by prescribing, dispensing and administering the drug to patients at Ra-Mar Clinic; that the defendant was aware that the promotion and use of a drug of this type in treating arteriosclerosis violated the law because he had been enjoined since 1976 in the Eastern District of Louisiana in connection with his use of a similar drug, edetate disodium, U.S.P., in such treatment; 502(f)(1).

The court denied the government's motion for a temporary restraining order, saying:

"This cause is now before the Court on the Plaintiff's motion filed herein March 19, 1978, for a temporary restraining order.

"An in-chambers conference and an extensive evidentiary hearing were held on the motion wherein all parties were present through counsel. Upon consideration of the motion, the pleadings and the testimony of witnesses, this Court finds that the testimony of the Government has not been sufficient to carry the burden of proof to establish by a preponderance of the evidence in the case the use by Dr. Evers of this drug and that, assuming the technicalities are as the Government has presented them, failure of proof is sufficient to defeat the appliance in this case of a temporary restraining order. The Court further finds that the Plaintiff has failed to demonstrate by a preponderance of the evidence a likelihood of success on the merits and an immediate threat of irreparable injury sufficient to warrant issuance of a temporary restraining order."

The government requested permission for FDA to enter the clinic for the purposes of an inspection and the obtaining of documents relating to: Ra-Mar Clinic patients; the purchase, order or receipt of chelating action drugs such as Edetate Calcium Disodium Injection, and ethylenediamine tetraacetate (EDTA); and written and printed descriptions of the Ra-Mar Clinic, the treatment offered at the Ra-Mar Clinic, chelation therapy, the treatment of arteriosclerosis and other cardiovascular diseases; and the use of EDTA drugs. Since counsel for the defendant had stated that the defendant was agreeable to such an inspection and the requested discovery was clearly proper, the court granted the motion requested by the government.

Ann H. Garrett and a number of patients of the defendant moved to intervene as a class of past and present patients of the defendant seeking declaratory judgment establishing their right to privacy as pertaining to their medical records, their right to choose the physician of their choice, and their right to choose the treatment, advice and counsel given by the physician of their choice, and also seeking injunctive relief in that the plaintiff not be allowed to inspect the medical records as described in the court's previous order.

The court granted the motion to intervene. After a hearing, the court denied the motion for a temporary restraining order prohibiting the plaintiff from inspecting and copying the defendant's medical records, saying:

"This cause is also before the Court upon the Defendant-Intervenors' motion received herein May 10, 1978, for a temporary restraining order prohibiting the Plaintiff from inspecting and copying Defendant's medical records. The matter was submitted on the pleadings after a hearing attended by counsel for all parties.

"The Defendant-Intervenors aver two grounds in support of their motion. They allege, first, that the law of Alabama prohibits Defendant Evers, a licensed physician, from disclosing his medical patient records to the Plaintiff. Second, they aver that these records fall within the constitutional right of privacy recognized by the United States Supreme Court in *Roe* v. *Wade*, 410 U.S. 113 (1972) and are, therefore, privileged from disclosure to the Plaintiff.

"This Court is not persuaded by these arguments. Under the decision of the Alabama Supreme Court cited by the Plaintiff, the Court recognized only a qualified privilege, stating: '. . . [I]t must be concluded that a medical doctor is under a general duty not to make extra-judicial disclosures of information acquired in the course of the doctor-patient relationship and that a breach of that duty will give use to a cause of action. It is, of course, recognized that this duty is subject to exceptions prompted by the supervening interests of society, as well as the private interests of the patient himself.' . . . The law of Alabama recognizes that the need for privacy and confidentiality must on occasion yield to significant social interests. The Supreme Court in *Roe* v. *Wade, supra*, recognized this need to balance public and private rights. In the opinion of this Court, the Government's need to assure that drugs are not being improperly misbranded supersedes the Defendant's and the Defendant-Intervenors' rights of privacy and confidentiality. There is, therefore, no likelihood of immediate or irreparable loss, injury or damage to which the Defendant-Intervenors are exposed."

Subsequently, in response to additional litigation, the court said:

"This cause is now before the Court upon the following motions: Defendant's motion to dismiss filed herein May 22, 1978; Defendant's motions filed herein May 22 and 23, 1978, for reduction of time within which the Plaintiff must answer interrogatories; motions of A. Roy Gary and Earl Davis filed herein May 23, 1978, pursuant to Rule 45(b), Federal Rules of Civil Procedure, to quash the subpoenas duces tecum served upon them May 23, 1978; motion of the Attorney General of the State of Alabama filed herein May 23, 1978, for a protective order relieving that office from compliance with the subpoenas duces tecum for a deposition by the Defendant on May 23, 1978; and the Defendant's motion filed herein May 23, 1978, for sanctions. A conference was held on these motions in chambers, wherein all parties were represented by counsel. Upon consideration of the motions, it is

"Ordered by this Court that the Defendant's said motion to dismiss and the Defendant's motion for sanctions be, and the same are hereby, denied. It is further

"Ordered by this Court that said motions for reduction of time be, and the same are hereby, granted, and the documents requested are hereby ordered to be produced by the Plaintiff on Tuesday, May 30, 1978, as agreed by counsel, and the Plaintiff is ordered to respond to said interrogatories on or before June 2, 1978. It is further

"Ordered by this Court that said motions of A. Ray Gary and Earl Davis to quash be, and the same are hereby, granted for want of adequate notice. It is further

"Ordered by this Court that said motion of the Attorney General of the State of Alabama for a protective order be, and the same is hereby, granted."

After the government had filed its answers to the defendant's interrogatories, the case came on for adjudication by the court. The court found for the defendant, saying:

"This cause is submitted upon the pleadings, the briefs, and evidence for final judgment. The Plaintiff, the United States of America, spear-headed by the Federal Drug Administration, filed this proceeding against Dr. H. Ray Evers, a licensed physician in the State of Alabama, alleging (1) that Defendant has been engaged in promoting and administering Calcium Disodium Versenate [calcium EDTA] in treatment for arteriosclerosis; (2) that the labeling of the drug, commonly called the package insert, which is prescribed and approved by the Federal Drug Administration, indicates that the drug is recommended for treatment for heavy metal poisons but not for other things here relevant; (3) that patients being treated by the Defendant are subjected to an unwarranted risk of grave physical injury or death as a result of said treatment; and (4) that the promotion and administering of said drug, after having utilized interstate commerce in obtaining the same, amounts to a mislabeling of the drug under the provisions of Title 21, U.S.C. §§331(k) and 352(f)(1). The Plaintiff contends that using chelating drugs in the treatment of arteriosclerosis and other cardiovascular problems creates a use for the drug for which it is not properly labeled, thereby misbranding or mislabeling the drug within the meaning of 21 U.S.C. §352(f)(1).

"The defense is that Defendant is not using the drug for other than treatment of metal poisoning, its recommended use, and that, in any event, the Defendant is a licensed physician in the State of Alabama and that licensed physicians have a right and a duty to use drugs in prescribing for their patients' usage in accordance with their best judgment as physicians and that the Federal Food and Drug Act does not prohibit a licensed physician's using a drug for a disease or weakness in a patient in any manner which is not contraindicated on the package insert.

"It is necessary in considering the issues in this case to have at least a lay conception of what the process of chelation amounts to in treatment of heavy metal poisons or for arteriosclerosis. Chelation involves intravenous injections in the patient of chemicals which tend to react chemically with the harmful metals which accumulate in and deter passage of blood within the blood vessels. Upon dissolution of these harmful substances by the chemical reaction to the chelating drug, the harmful metals are dissolved and pass out of the body through the kidneys. The danger involved is that too many of such substances may be passed into the kidneys too rapidly and, on occasion, renal poisoning sets in, and kidney failure results in the death of the patient. The danger associated with the harmful metals remaining in the blood vessels is that the blood vessel may become clogged, disallowing free passage of the blood through the blood vessels and cause stroke, diminished ability to reason or remember (senility) because of inadequate blood supply to the brain, gangrene resulting from failure of sufficient blood in the limbs, and various degrees of numbness, dizziness and pain associated with failure of circulation.

"The Defendant explains that his method of chelation originally involved the intravenous injection of a chelating drug (disodium EDTA, which he no longer uses) mixed with vitamins and minerals designed to maintain the strength of the patient and the proper mineral balance within the patient's body. He insists that each patient who comes into his clinic is given extensive tests to determine the mineral (good and bad) content of the body and that he mixes the injectables to replace the needed trace minerals and to dissolve the harmful mineral content in the fluids of the body.

"The alternative treatment for arteriosclerosis is by-pass surgery and one danger associated with Defendant's treatment, according to Plaintiff, is that persons will be delayed beyond the point of no return to surgery by first resorting to Defendant's treatment.

"The relief sought by the Plaintiff is that this court grant an injunction restraining (1) The receipt or possession of disodium edetate, calcium disodium edetate, or any other drug possessing chelating action by the Defendant; (2) The continuance of administration of chelating therapy by the Defendant; and (3) The allowance of regular inspection of Defendant's clinic by the Federal Drug Administration.

"It must be borne in mind that there are a number of things which this suit is not. This is not a suit for malpractice by the Defendant nor a proceeding to enjoin false advertising. It is not a proceeding to cancel the license to practice medicine of the Defendant nor is this court authorized to invoke such a remedy. It is also not a suit challenging the Defendant for failure to use an obvious cure for a known disease or weakness. This is also not an attempt to enjoin Dr. Evers from administering intravenous injections of vitamins and minerals to his cardiovascular or other patients. While the government suggests that this treatment for cardiovascular patients is without value and could be harmful, these concerns are not within the purview of this lawsuit. This court derives its power from the clause of the Constitution granting the United States authority over interstate commerce and jurisdiction of this court is so limited.

“The legal issues presented by this cause, in the opinion of this court, place squarely before this court the question of whether a licensed physician may be enjoined from prescribing for his patients a drug of which the package insert is silent as to whether the drug is indicated or contraindicated for the patient's illness.

“Several recognized factors which the court should keep in mind is that the decision making power of a physician may involve a consideration of the possible curative value of not notifying a patient of all of the risks associated with the use of a drug or indicated on the package insert on the drug prescribed for that patient. In the opinion of this court, that decision must be a professional one made by the physician himself. This court finds from the evidence that Dr. Evers, before using EDTA, did not always inform his patients of the risks shown on the package insert to have been associated with the use of calcium EDTA as a chelating agent. The Court will also keep in mind the well-known medical fact proved by several physicians in testimony in this proceeding that, of all patients treated by physicians, a large majority would recover no matter what treatment is provided therefor. However, this majority is obviously not applicable to those suffering from advanced arteriosclerosis wherein the patient may expect an early disabling resulting from stroke, hypertension, heart failure, or other related diseases or cardiovascular problems.

“A part of the defense of Dr. Evers is that no scientific person would attempt to chelate for arteriosclerosis with calcium EDTA. The well-supported theory is that calcium is an element which tends to accumulate in the blood vessels and that the calcium in the calcium EDTA would not tend to chemically react with the calcium in the blood vessels materially so as to achieve dissolution of the deposits within the blood vessels commensurate with action by other chelating agents not having high calcium content. However, Dr. Evers admits that, in treating for a metal toxicity, such as lead, patients who also have arteriosclerosis, he has found that chelation with calcium EDTA has proven effective to aid, not only the heavy metal poison but also, the arteriosclerosis. He explains that the metal content of the blockage in the arteries is neutralized by the chelating agent and passes out of the blood and that the calcium deposit remaining in the blood vessels, having lost its mineral structural balance, tends to disintegrate and pass out through the kidneys along with other undesirable elements. He compares it with the failure of a structural building once the metal supports therein have been removed. It is therefore clear that, while Dr. Evers preferred another chelating agent for arteriosclerosis, he admits a large degree of success in treating arteriosclerosis victims with calcium EDTA. He is now of the opinion that no chelating agent is necessary for arteriosclerosis as the treatment may be accomplished through intravenous injections of minerals and vitamins without a chelating agent. This suit poses no threat to such treatments for arteriosclerosis or other disease.

“It is well-established by the evidence in this case and by the package insert that the danger associated with the use of chelating drugs is kidney failure resulting in death. It is therefore not surprising that no former patient of the subject physician survives to testify against his use of chelating drugs. It is also well-established that there have been no controlled scientific tests in this country which have demonstrated that chelation therapy with calcium EDTA has been successful in treatment of cardiovascular disease. However, the favorable lay support of chelating drugs from former patients relieved by the Ever system of the obvious symptoms of arteriosclerosis, together with testimony from a few doctors and osteopaths who have used the treatment, cannot be ignored. Irrespective of the strong medical school of thought that chelation has not been clinically shown to help arteriosclerosis, the weight of the evidence submitted to this court is to the contrary.

“While the primary school of thought in the southeast among reputable medical practitioners is that chelation therapy is not a proper treatment for arteriosclerosis and that use of chelating drugs is a dangerous practice which may cause renal failure and death from kidney poisoning, there is clearly a school of thought to the contrary. Several Western physicians and doctors of osteopathy testified to success in chelation therapy for cardiovascular problems and one doctor indicated it to be the preferred treatment in at least one European country. While the Evers school feels that chelation is a proper treatment for arteriosclerosis, they do not question that a potential danger thereof is kidney poisoning if the drugs are not properly administered. They and Dr. Evers insist, however, that they have administered large quantities of the drugs and that, if regular and proper urine analyses are maintained and if the patient is taken off the drug if it appears that excessive minerals are accumulating in the kidneys, there is little danger of kidney failure in an otherwise healthy patient. They, of course, recognize that occasionally arteriosclerosis has progressed to such a stage that the patient is extremely weak, advanced in age, or his kidneys are already weak and in such instances the risk of any treatment may exceed the potential value thereof. The problem for the physician, as in most serious cases, is to weigh the possible benefits of treatment against the possible risks. The Defendant insists that chelation therapy is the best treatment for even the more advanced stages of cardiovascular disease and the risks and the wear and tear on the patient are less than those associated with by-pass surgery.

“The first defense is that the defendant uses calcium EDTA only for treatment of heavy metal poisons and has not used it in treatment of purely arteriosclerosis. This court is of the opinion that the weight of the evidence is to the contrary.

“Government agents, examining the files of about 600 of the more recent patients treated by Dr. Evers found that the records of the Ra-Mar Clinic, where Dr. Evers practices, indicated that 72 patients had received chelation therapy involving the use of calcium EDTA. Of this group nearly all had a diagnosis of arteriosclerosis but only 31 had a diagnosis or showing of any lead or heavy metal content whatsoever. While Dr. Evers contends that the presence of any amount of the toxic metals shown by analysis justifies treatment thereof, it appears that over 40 of the patients receiving the chelation treatment showed no heavy metal content in the tests shown on their charts. Additionally, it appears that during the time in question, 2,028 grams of calcium EDTA was received by the Ra-Mar Clinic and that patients were usually treated at 1 gram per person per day for 21 days. At the rate of 21 grams per patient for the 31 'lead' patients, the lead patients would have received a total of 1,611 grams of calcium EDTA. With a showing of little calcium EDTA inventory, a difference of about 1,017 grams (2,628 minus 1,611) of calcium EDTA remains unaccounted for. Assuming that patients receive the usual dose of 21 grams per 3-week period, 1,017 grams would provide the routine dose (Evers) for approximately 48 patients (1,017 grams divided by 21 grams—the average dose per patient) who appear to have been chelated with calcium EDTA but whose records of metal poison are unaccounted for. Since the dose is not always the usual, it is reasonable to assume from either of the above calculations that about 40 patients of the 72 who received calcium EDTA had absolutely no diagnosis of a heavy lead poison. While this court is aware and judicially knows that some mistakes do occur in most records, Dr. Evers, warned by prior problems associated with his insistence upon the propriety of chelation as treatment for arteriosclerosis, could hardly be expected to not understand the value of his keeping records associated with his establishment of proof that a chelating agent was being properly used. The disparity between the nurses' testimony about the incidence of lead poison among patients, the statements by a few patients that they received chelation therapy from Dr. Evers, and the advertisement by Evers of chelation therapy are consistent with the availability at Ra-Mar Clinic of chelation therapy for cardiovascular problems. While the FDA has the burden of proof in these cases, the associated facts convince this court that Dr. Evers has offered chelation therapy associated with use of calcium EDTA to arteriosclerosis patients at Ra-Mar Clinic. The Plaintiff contends, and this court found, that Dr. Evers has during the past two years offered chelation therapy using calcium EDTA as his chelating agent to arteriosclerosis patients at Ra-Mar Clinic, that he has ordered and received interstate shipments of calcium EDTA for use in said treatments during said period of time, and that he has advertised in interstate commerce his use of chelating agents as treatment for arteriosclerosis. It is agreed that chelation therapy with calcium EDTA is neither indicated nor contraindicated on the package label for said drug. While there have been no controlled clinical tests which indicate either the reliability of chelation therapy in treating arteriosclerosis or the danger thereof while properly supervised, the weight of medical opinion in the United States, and almost the unanimous medical opinion in the Southeast, is that chelation therapy is of no benefit for treatment of arteriosclerosis and that such treatment is dangerous both in the fact that it may result in kidney failure and in the fact that it may cause the patient to delay the alternative treatment of by-pass surgery to the extent that the patient may lose his life when proper action might save it.

"The court is of the opinion, however, that there is a school of thought among medical experts in this and some foreign countries that arteriosclerosis may be satisfactorily treated with chelation therapy, that the risks when the therapy is properly administered to selected patients are minimal and that in many cases the probable benefits outweigh the probable risks in such treatment. The Evers proponents take some consolation in the fact that the Plaintiff's experts opposing the Evers method rely upon textbook learning whereas the people who have approved the Evers method are people who have had personal experience with chelation following the Evers school of thought and have found it successful even though they do not profess to have conducted any controlled clinical evaluation thereof such as is ordinarily required by the Federal Drug Administration for approval of a new drug.

"The government contends, and most experts agree, that calcium is not a cause of, nor is it universally associated with, the development of arteriosclerosis and that there is no known method of removing calcium from the arterial wall. The Plaintiff's expert physicians, all of whom are competent and well-recognized in this section of the country, disagree with the Evers theory that arteriosclerosis can be cured by removing excess calcium from the arteries. Even the Defendant's witnesses concur that calcium disodium versenate is not the proper chelating agent to remove calcium from the arteries. However, Dr. Evers contends that, while calcium disodium versenate is not the preferred chelating agent, that the minerals are removed by chemical reaction and the washing of the arteries with the compounds of intravenous injectables which he uses and that once the minerals are removed the calcium tends to be removed with them.

"In response to Dr. Evers' contention that the Federal Drug Administration has no power to direct how he shall treat his own patients, the government relies upon *United States* v. *Hoxsey Cancer Clinic*, 198 F.2d 273 (5th Cir. 1952), in which a layman, Hoxsey, was advertising and shipping drugs in interstate commerce as a cancer cure and the court found that the literature distributed constituted mislabeling of the drugs within the meaning of the act because it contained misleading statements and therefore the drugs were misbranded and Hoxsey was enjoined from the continuation of such interstate commerce. The Hoxsey case is comparable to the instant case in that the Hoxsey Clinic was staffed by licensed physicians but Hoxsey was shipping the drugs in interstate commerce to other than his patients after having advertised them for unapproved usage while Dr. Evers, after having received a drug in interstate commerce, holds them for prescribed use on his patients. As pointed out in Hoxsey, 'We do not attempt to set ourselves up as arbiters of what method of treatment the Hoxsey Clinic should employ. We are not authorized by law to do so. It is our duty to adjudge the merits of the case in light of the provisions of the Federal Food, Drug, and Cosmetic Act, *supra*, which closed the channels of interstate commerce against drugs that are misbranded.' (At page 281)

"The government also relies on the case of *United States of America* v. *An Article of Drug * * * Diso-Tate, Etc., H. Ray Evers, and Meadowbrook Hospital*, No. 75–1790 (E.D. La., Sept. 28, 1976), in which Judge Gordon enjoined the Defendant in this case from indulging in chelation therapy with disodium edetate as treatment for arteriosclerosis in Louisiana. In that case, Dr. Evers again was advertising in interstate commerce and receiving shipments of drugs to effect the chelation of patients as a treatment for arteriosclerosis. Two obvious differences appeared in that case as compared with the instant case. The drug used for chelation in Louisiana was contraindicated for arteriosclerosis on the label and Dr. Evers himself was not a licensed physician and was operating as a layman in Louisiana. That case, therefore, has limited authority in the instant case. It is notable, however, that that court expressed its concern about any unwarranted interference with the practice of medicine even though Dr. Evers was not licensed to practice in Louisiana at that time.

"The government also relies on the cases of *United States* v. *Collier*, 478 F.2d 268, and *United States* v. *Moore*, 423 U.S. 122. The Collier case is inapplicable in that the physician was charged with distributing a controlled substance in excess of the moderate amount which he might have prescribed for a patient to treat addiction or to relieve conditions of suffering incident to addiction. The court readily recognized that a physician cannot, under the guise of practicing medicine, sell drugs to a dealer or distribute drugs intended to cater to the cravings of an addict. The case of *United States* v. *Moore, supra*, is equally inapposite in that the doctor in that case was distributing a controlled substance, an addictive drug used in the treatment of heroin addicts, that he was prescribing large quantities of methadone for patients without giving them adequate physical examinations or specific instructions for its use and that he charged fees according to the quantity of methadone prescribed rather than fees for medical services rendered. The court concluded that he was using his medical license as an excuse for sale of illicit drugs to addicts and was therefore in violation of the law. The statute under which each of these doctors was tried allowed reasonable dispensation of these drugs in question for normal medical practices.

"In the opinion of the court the government's strongest position comes from the FEDERAL REGISTER. 37 Fed. Reg. 16503–05 provides that a physician is not required to file an investigational new drug plan before prescribing an approved drug for non-approved use but that the Food and Drug Administration does have duties when it appears that the unapproved use of an approved new drug becomes widespread or endangers the public's health. When a manufacturer or anyone in the chain of distribution suggests to a patient that an approved drug may properly be used for unapproved uses for which it is neither labeled nor publicly advertised, that action constitutes a violation of the action and is punishable accordingly as a misbranding of the drug. The government contends that a physician or other person who ships or requests shipment of a prescription new drug in interstate commerce with the intent of applying it to an unapproved use, that person must first file with the Food and Drug Administration an investigational new drug plan as set out in 21 CFR, §312.1. Nonetheless, if a new drug has been shipped in interstate commerce intended for its approved use, a physician is not required to file an application for a new drug plan if he prescribes the drug as part of the practice of medicine. A possible violation may arise from the purpose of the person causing the drug to be shipped in interstate commerce. The Plaintiff admits that the government cannot regulate the practice of medicine by any licensed physician but it contends that it can prohibit the use of interstate commerce in transportation of drugs for usages not approved by the Federal Drug Administration.

"Perhaps the government's position is best exemplified by the explanation of the purposes of the Federal Food and Drug Administration's interest in practices such as those enjoyed by Dr. Evers in the FEDERAL REGISTER for August 15, 1972 (Vol. 37, No. 150, P. 16503). That position is that once a drug is in a local pharmacy, after interstate shipment, a physician may, as part of the practice of medicine, lawfully prescribe a different dosage for his patients or may vary the conditions of use from those approved in the package insert, without informing or obtaining the approval of the Food and Drug Administration. Congress did not intend the Food and Drug Administration to interfere with medical practice as between the physician and the patient. Congress recognized a patient's right to seek civil damages in the courts if there should be evidence of malpractice, and declined to provide any legislative restrictions upon the medical profession. It appears to this Court that such a restriction would exceed the powers of Congress. There is no federal prohibition of transportation of an approved drug in interstate shipment with the approved package insert when neither the shipper nor the recipient intends that it be used for an unapproved purpose. If the illegal purpose is devised after termination of interstate shipment, the matter has passed from federal jurisdiction, but jurisdiction may well apply if the shipper or the recipient intends an illegal use at the time of the deposit of the shipment in interstate commerce. Then the act and the illegal intention may coincide so as to furnish federal jurisdiction over interstate commerce.

"In the case of *F.T.C.* v. *Simeone Management Corporation*, 532 F.2d 708 (1976), the Court pointed out that, if a drug that has FDA approval for specific uses is used by a treating and prescribing physician for an unapproved use, this is not considered a new drug use that would require the physician to file an investigational new drug plan or to submit a new drug application. The Court pointed out that the physician may, as part of the practice of medicine, lawfully prescribe a different dosage for his patient or may otherwise vary the conditions of use from those approved in the package insert without informing or obtaining the approval of the Food and Drug Administration.

"Congressional intent set out in 37 Fed. Reg. 16503 (1972) indicates that Congress did not intend the Food and Drug Administration to interfere with medical practice and that the bill did not purport to regulate the practice of medicine as between the physician and the patient.

"It is well-recognized that a package insert may not contain the most up-to-date information about a drug and the physician must be free to use the drug for an indication not in the package insert when such usage is part of the practice of medicine and for the benefit of the patient. Hopefully the physician would welcome a well-documented package insert because he finds it useful because the information in it is supported by substantial documented evidence. However, the physician can ascertain from medical literature and from medical meetings new and interesting proposed uses for drugs marketed under package inserts not including the new proposed usages. The package insert's most important educational value derives from the fact that it is a well-reviewed, authoritative document. New uses for drugs are often discovered, reported in medical journals and at medical meetings, and subsequently may be widely used by the medical profession. But the Federal Drug Administration does not permit the package to be amended to include such uses unless the manufacturer submits convincing evidence supporting the change. The manufacturer may not have sufficient commercial interests or financial wherewithal to warrant following the necessary procedures to obtain FDA approval for the additional use of the drug. When physicians go beyond the directions given in the package insert it does not mean they are acting illegally or unethically and Congress did not intend to empower the FDA to interfere with medical practice by limiting the ability of physicians to prescribe according to their best judgement. See FDA CONSUMER, November 1975, page 8.

"The Supreme Court, in *Linder* v. *U.S.*, 268 U.S. 5 (1925), stated the following: 'Obviously direct control of medical practice in the States is beyond the power of the federal government. . . . It (the statute) says nothing of "addicts" and does not undertake to prescribe methods for their medical treatment. They are diseased and proper subjects for such treatment, and we cannot possibly conclude that a physician acted improperly or unwisely or for other than medical purposes. . . . What constitutes bona fide medical practice must be determined upon consideration of the evidence and attending circumstances.' 268 U.S. at 18. The courts have rather uniformly recognized the patients' rights to receive medical care in accordance with their licensed physician's best judgment and the physician's rights to administer it as it may be derived therefrom. See *Dog* v. *Bolton*, 410 U.S. 179, 197 (1973); *Whalen* v. *Roe*, 429 U.S. 589 (1977). The Supreme Court in *Doe* v. *Bolton*, *supra*, observes that if a physician is licensed by the state, he is recognized by the state as capable of expressing acceptable clinical judgment. If he fails in this, professional censure and deprivation of his license are remedies available and reliance must be placed on the assurance given by his license that he possesses the requisite qualifications. Obviously the physician's failures are also subject to the ever increasing possibilities of malpractice suits in current times. In *Roe* v. *Wade*, 410 U.S. 113, (1973), the court in approving the patient's right to an abortion prescribed by her physician stated that, 'To require prior State approval before advising, prescribing, administering a new treatment medically for an informed consenting patient is to suppress innovation by the person best qualified to make medical progress. The treating doctor, the clinician, is at the cutting edge of medical knowledge.

" 'To require the doctor to use only orthodox "State sanctioned" methods of treatment under threat of criminal penalty for variance is to invite a repetition in California of the Soviet experience with Lysenkoism. The mention of a requirement that licensed doctors must prescribe, treat, within State sanctioned alternatives raises the spector of medical stagnation at the best, statism, paternalistic big brother at worst. It is by the alternatives to orthodoxy that medical progress has been made. A free, progressive society has an enormous stake in recognizing and protecting this right of the physician.'

"This court is, therefore, of the opinion from the pleadings, the evidence and the authority presented to it that Dr. Evers is not misbranding the drug in question and that the relief prayed by the plaintiff should be denied. Judgment will enter in accordance with this memorandum opinion.

"The government appealed. Upon appeal, the U.S. Circuit Court of Appeals for the Fifth Circuit affirmed the judgment of the district court in favor of Dr. Evers, saying: 'We do not reach the issue on which the district court's opinion rests, for we find that the government has not established a violation of section 301(k) of the Act. Since prescription drugs are required by regulations promulgated pursuant to section 502(f)(1) of the Act to bear adequate information for use by physicians but not for use by patients, and since the physician charged in this case was administering the drug to his own patients but not distributing it to other physicians, we hold that Dr. Evers has not violated section 301(k) of the Act by his failure to provide such 'adequate directions for use' as are required by section 502(f)(1) of the Act. We therefore affirm the judgment of the district court in favor of the defendant.'

I. THE FACTS

"Dr. H. Ray Evers is the owner and operator of Ra-Mar Clinic, a health facility which opened in 1976 in Montgomery, Alabama. Dr. Evers and his clinic specialize in the treatment of chronic degenerative diseases. Although the clinic is not a hospital, it has a 40-bed capacity and does accept patients for treatment on a resident basis for periods of up to three or four weeks.

"A central part of Dr. Evers' approach to the treatment of degenerative diseases is his use of 'chemo-endartectomy therapy.' Dr. Evers explains this therapy as 'a special treatment given by licensed medical doctors for the relief of poor circulation that has been caused by hardening of the arteries (arteriosclerosis, atherosclerosis).' Dr. Evers' approach, which he describes as 'wholistic' and 'preventative,' seeks to alleviate circulatory disorders by creating the proper balance of metals, vitamins, enzymes and other substances in the body.

"The most important part of Dr. Evers' chemo-endartectomy therapy is his use of 'chelation.' Chelation is a chemical reaction which occurs between certain drugs and various harmful metals which are in the bloodstream. These drugs, which Dr. Evers injects intravenously, form a bond with heavy metals in a form which allows them to pass out of the body through the kidneys. Chelating drugs are ordinarily used for the treatment of heavy metal poisoning, particularly lead poisoning. According to Dr. Evers, however, this process also removes from blood vessels buildups of calcium which are blocking the vessels and causing hardening of the arteries. Dr. Evers claims that he has used chelation therapy with tremendous success in the treatment of circulatory disorders, and with little danger to his patients. . . . 'Whether this process actually has this beneficial effect is a serious question. Dr. Evers' claims for his therapy are not generally accepted by the medical profession, and . . . the FDA has not approved any chelating drug for use in the treatment of circulatory disorders. . . .

"The focus of the government's case against Dr. Evers is not, however, the potential danger in his use of chelation therapy. Instead, the government challenges his vigorous promotion and advertising of chelating drugs for a use which has not been approved by the FDA. As the district court found, Dr. Evers 'advertised in interstate commerce his use of chelating agents as treatment for arteriosclerosis.' 453 F. Supp. at 1146. Unfortunately, the district court did not discuss this crucial aspect of Dr. Evers' operation in any greater detail. Nevertheless the record clearly indicates the seriousness of Dr. Evers' promotional efforts. When the Ra-Mar Clinic opened in 1976, Dr. Evers placed a full two-page advertisement in the MONTGOMERY ADVERTISER. Although the ad did not explain Dr. Evers' program in any detail, it specifically listed chemo-endartectomy therapy as one of his chief methods. The more important aspect of Dr. Evers' campaign, however, consists of a booklet describing the Ra-Mar Clinic. The booklet explains chemo-endartectomy and chelation in lay terms and describes the program employed by the Ra-Mar Clinic. The booklet claims remarkable success for chelation, cites Dr. Evers' extensive experience with the process, urges the reader to try chemo-endartectomy therapy before traditional modes of treatment, and underplays the serious dangers involved in the use of chelating drugs. This booklet was apparently given to patients and prospective patients of the clinic, both in person and through the mail. Although the district court does not appear to have addressed the extent of this distribution, the government did introduce testimony which suggests that as many as 4,000 of these booklets may have been distributed through the mail. Trial Transcript at 218–20. While we cannot trace with precision the particular promotional efforts undertaken by Dr. Evers, it is at least clear from the record that Dr. Evers did, as the government alleges, promote and advertise his use of chelating drugs for the treatment of circulatory disorders.

"Although there exists a variety of lawful chelating drugs, the government has charged Dr. Evers in this suit with the misbranding of one particular chelating drug, calcium disodium edetate (Calcium EDTA). Dr. Evers argued in the district court that he did *not* use this drug for the treatment of arteriosclerosis or other circulatory diseases, but rather only for the treatment of heavy metal poisoning. In fact, Dr. Evers introduced evidence to the effect that Calcium EDTA would be ***absolutely ineffective*** in the treatment of circulatory disorders since it could not bind with calcium, which, according to his theory, is the cause of artery obstructions. Trial Transcript at 330–31, 534–35. Accordingly, Dr. Evers contended that neither he nor any other proponent of chelation therapy had used Calcium EDTA for the treatment of circulatory disorders. *Id.* However, an examination of medical records at the Ra-Mar Clinic demonstrated that 72 patients had received chelation therapy with Calcium EDTA; nearly all of this group had a diagnosis of arteriosclerosis but only 31 patients had a diagnosis showing any lead or other heavy metal content whatsoever. 453 F. Supp. at 1146. On this basis the district court concluded that Dr. Evers during the two years before trial had indeed 'offered chelation therapy using Calcium EDTA as his chelating agent to arteriosclerosis patients at Ra-Mar Clinic . . .' *Id.* This finding is not challenged by Dr. Evers on an appeal.

"The district court also found that the FDA-approved labeling (commonly called the package insert) for Calcium EDTA does not indicate that the drug can be used to treat circulatory diseases and does not include any instructions for the use of the drug for such purposes. *Id.* In fact, the sole purpose indicated on the label for Calcium EDTA is 'the reduction of blood levels and depot stores of lead in lead poisoning (acute and chronic) and lead encephalopathy.' The FDA is therefore correct in its assertion that, whether or not chelation is of any beneficial effect to a patient suffering circulatory diseases, the package insert in the Calcium EDTA used by Dr. Evers provided no direction whatsoever for that use of the drug.

II. THE GOVERNMENT'S CASE AGAINST DR. EVERS

"The government contends that Dr. Evers violated section 301(k) of the Act, 21 U.S.C. § 331(k), which prohibits any act with respect to a drug which 'is done while such [drug] is held for sale (whether or not the first sale) after shipment in interstate commerce and [which] results in such article being . . . misbranded.' . . .

"The object of the government's case against Dr. Evers is not, therefore, his *prescription* of Calcium EDTA for use in the treatment of circulatory disorders. Instead, the government seeks to challenge Dr. Evers' *promotion* and *advertising* of chelating drugs for that use. According to the government, Dr. Evers 'misbranded' Calcium EDTA when he publicly advocated his use of chelating drugs for an unapproved purpose without providing 'adequate directions' for such a use. . . .

"Since the government relies for its case on Dr. Evers' promotion and advertising of chelating drugs for an unapproved use, and since the FDA itself interprets the Act to allow physicians to prescribe (while not promoting or advertising) lawful drugs for unapproved uses, we need not decide whether, as the district court apparently concluded, the constitution prohibits federal interference with prescriptions by licensed physicians. The question before us is the narrower issue of whether Dr. Evers violated section 301(k) of the Act. In order to establish such a violation, the government must demonstrate the two elements required by that section. In terms of this case, we must find (1) that Dr. Evers held Calcium EDTA for sale after its shipment in interstate commerce, and (2) that Dr. Evers' promotion and advertising of Calcium EDTA without providing any more information than was contained on the drug's label and in the clinic's pamphlets failed to provide 'adequate directions for use' and therefore constitutes misbranding under section 502(f)(1) of the Act.

III. THE GOVERNMENT'S APPLICATION OF THE ACT, OR, WHY THE STATUTE DOES NOT FIT THE FACTS

A. Section 301(k): Extending the Act to Drugs 'Held for Sale after Shipment in Interstate Commerce'

"The Act was intended, *inter alia*, to keep misbranded drugs out of the channels of interstate commerce. The flow of commerce begins with the manufacturer of the drug and ends with the consumer, that is, the patient. Accordingly, section 301 of the Act is designed to prevent misbranding at each stage of the distribution process. . . .

"The gap which section 301(k) was designed to fill arises when a drug which has already been transported in interstate commerce is misbranded by a person who neither shipped nor received the drug in interstate commerce. . . . Section 301(k) extends the Act's protection to the entire distribution process for drugs moving in interstate commerce by covering what is often the final stage in that process: the distribution by a person not himself a party to the interstate transportation of the drug.

"This final stage of the distribution process, where drugs are 'held for sale after shipment in interstate commerce,' takes on many different forms. The statute has been construed to cover situations in which the drugs are held by a retailer, . . . a wholesaler . . . and a bailee. . . . A practicing physician may also fall within the bounds of this section. A serious gap would be left in the statute if doctors who had received drugs in an intrastate transaction from a party who had in turn received them from interstate commerce were allowed to misbrand the drugs and then distribute them to their patients. Doctors holding drugs for use in their practice are clearly one part of the distribution process, and doctors may therefore hold drugs for sale within the meaning of section 301(k) of the Act. . . .

B. Misbranding Under Section 502(f)(1)

"We now turn to the second requirement of section 301(k) in the context of this case: the drug at issue must have been misbranded. In order to establish that Dr. Evers misbranded Calcium EDTA, the government relies on section 502(f)(1) of the Act, 21 U.S.C. § 352(f)(1). . . .

"A two-fold scheme emerges from section 502(f)(1) when it is read in the context of the FDA's interpretation of the 'adequate directions for use' requirement and of the regulatory and statutory exceptions to that requirement. If the drug is a non-prescription drug, the distributor must provide adequate directions in lay terms to the patient himself. But if the drug is a prescription drug, as is Calcium EDTA, the distributor must provide the information which is required by the regulatory or statutory exception to the statute, for it is impossible for the distributor to adequately explain a prescription to a layman. Thus, neither prescription nor non-prescription drugs can meet the terms of the statute by providing such 'adequate directions for use' as are required for the other type of drug.

"The purpose of this scheme is, in brief, to require that adequate information be provided to the person who must decide whether and how to administer the drug. Where non-prescription drugs are involved, the 'adequate directions for use' requirement insures full disclosure to the layman purchasing the drugs for self-treatment. But prescription drugs depend for their safety and effectiveness on the professional judgment of a licensed physician. Accordingly, the prescription drug exceptions to the 'adequate directions for use' requirement contain conditions requiring adequate information for prescribing doctors. . . .

C. Putting Together the Two Elements of Section 301(k)

"The government argues that Dr. Evers' prescription and promotion of Calcium EDTA for the treatment of circulatory disorders meets both of the above requirements of section 301(k) of the Act. In the first place, the government contends that Dr. Evers 'held [Calcium EDTA] for sale' when he maintained a supply of the drug for use on his own patients at the Ra-Mar Clinic. To support this position, the government relies on cases, cited in part III(A) of this opinion, which did indeed hold that a doctor who had held drugs for use in his practice had held those drugs for sale within the meaning of the Act. In the second place, the government contends that Dr. Evers misbranded Calcium EDTA within the meaning of section 502(f)(1) of the Act by failing to provide 'adequate directions for use' either in appropriate lay terms or according to the disclosure requirements of either exemption for prescription drugs. It is undisputed that Dr. Evers did in fact fail to provide adequate directions for either lay or professional use; Dr. Evers does not contend that his booklets contained 'adequate directions for lay use' within the meaning of the regulations, and he does not appear to have made any attempt to meet the terms of either the regulatory or the statutory exception for prescription drugs.

"When each of the two elements of the offense with which Dr. Evers is charged is examined individually, Dr. Evers does indeed seem to have violated the statute. A different picture emerges, however, when the two elements are considered together. Since Calcium EDTA is a prescription drug, the FDA can establish an act of misbranding under section 502(f)(1) of the Act only by proving that Dr. Evers did not provide adequate information *for use by physicians*, as is required by the exceptions to that section. The information provided by Dr. Evers to his patients is irrelevant to the question at hand, for according to FDA regulations there is *no* information which could have been provided about this prescription drug which would have constituted 'adequate directions for [lay] use.' However, the government argues that Dr. Evers 'held [Calcium EDTA] for sale' within the meaning of section 301(k) because he maintained a supply of the drug for use *on his own patients;* the government does not contend that Dr. Evers was distributing Calcium EDTA to other licensed physicians. The government therefore must find itself in an awkward position: while the misbranding violation it urges is based on Dr. Evers' failure to provide adequate information to licensed physicians, it seeks to include his actions within the reach of section 301(k) of the Act by virtue of his distribution to patients.

"The requirement which FDA seeks to impose is nonsensical. Since Calcium EDTA is a prescription drug, the misbranding provision under which Dr. Evers was charged requires him to provide adequate information for use by prescribing physicians. However, Dr. Evers was the only physician who used the Calcium EDTA in question. The government's application of the statute may therefore be reduced to the following proposition: Dr. Evers did not provide adequate information to himself. It is doubtful at best that this interpretation was intended by the drafters of the statute.

"In more specific terms, the government's interpretation of the Act breaks down over its use of the phrase 'held for sale after shipment in interstate commerce.' Although Dr. Evers was holding Calcium EDTA for sale in the sense that he was distributing it *to his own patients*, he was not holding it for sale *to physicians*. Section 301(k) of the Act cannot reasonably be read to require a physician who is holding a drug for sale only to patients to provide adequate information to physicians to whom he is not distributing the drug. We think it clear that a single doctor may be holding drugs for sale to one group of purchasers but not to another. If the doctor is not holding the drug for sale to the party to whom he owes a statutory obligation of full disclosure (in this case other prescribing physicians), then it makes no sense to impose the requirements of the statute. No legitimate purpose is served when a statutory provision requiring disclosure to one particular group of purchasers is invoked on the basis of sales made to a different group. Since Dr. Evers was holding Calcium EDTA, a prescription drug, for sale only to his patients, and since section 502(f)(1) of the Act does not require any disclosure to patients regarding prescription drugs, we conclude that Dr. Evers did not violate Section 301(k) of the Act.

IV. CONCLUSION

"We have not been called upon in this case to consider the safety and effectiveness of Dr. Evers' use of chelation therapy; accordingly, we neither approve nor criticize his medical practices. Nor have we been asked to decide whether Dr. Evers has violated the Federal Food, Drug, and Cosmetic Act on any basis other than that on which the government has built its case. The issue before us is a narrow one: whether Dr. Evers has violated section 301(k) of the Act by his failure to provide such 'adequate directions for use' as are required by section 502(f)(1) of the Act. Since Dr. Evers was not holding Calcium EDTA for sale to other prescribing physicians, the sole basis of the government's misbranding charge is Dr. Evers' failure to label the drug for physicians in accordance with either exception to section 502(f)(1) of the Act, we must conclude that the government has failed in this case to establish a violation of section 301(k) of the Act. We therefore affirm the judgment of the district court in favor of Dr. Evers." (Inj. No. 837; S. No. 78–127–637 et al.; N.J. No. 24)

Ronald K. Johnson, t/a Johnson Candy Co., Takoma, W. Dist. Wash.
Charged 3–17–78 in a complaint for injunction: that the defendant was engaged at his Tacoma, Wash., plant in manufacturing, processing, packing, holding for sale after interstate shipment of components, and shipping in interstate commerce candy and nut products which contained insect filth and which had been prepared, packed and held under insanitary conditions; that FDA analyses found insect fragment in samples of candy; that FDA inspections disclosed a number of specified insanitary conditions and practices; and that defendant was well aware that his activities were in violation of the law; 402(a)(3) and (4).

Consent decree of permanent injunction enjoined the complained of violations and enjoined operations involving interstate products unless and until a number of specified conditions were met. (Inj. No. 845; S. No. 78–149–104; N.J. No. 25)

Villalba Vegetable Growers Cooperative Assn., and **Victor M. Miranda,** administrator, and **Cesar R. Guzman,** plant manager, Villalba, Dist. P.R.
Charged 11–7–78 in a complaint for injunction: that, at the defendant's food cannery at Villalba, P.R., pink beans, red kidney beans, small whole beans and early June peas were prepared, packed and held; and a number of such thermally processed low-acid canned foods were held for sale after shipment of their interstate components; that such canned foods had been prepared, packed and held under insanitary conditions whereby they may have been rendered injurious to health because they had not been processed in compliance with regulations; that FDA inspections disclosed a number of specified failures to comply with good manufacturing practice regulations for low-acid canned food; and that the defendants were well aware that their activities were in violation of the law; 402(a)(4).

A consent decree of permanent injunction enjoined the complained of violation and enjoined the continued operation and distribution of such canned foods unless and until the requirements of good manufacturing practice were met, the cannery and its equipment were inspected and certified as being in compliance, all foods on hand were evaluated as to being in compliance, and all foods evaluated as having received a thermal process less than necessary to protect the public health were destroyed or otherwise brought into compliance. (Inj. No. 831; S. No. 78–157–206 et al.; N.J. No. 26)

Wallace Grain Co., Inc., and **Phil G. Wallace,** president and **United Feeds, Inc.,** and **H. Marshall Adkins,** secretary and treasurer, and **John B. Swisher,** president, Sheridan, S. Dist. Ind.
Charged 3–30–78 in a complaint for injunction: that Wallace Grain Co., Inc., and its named officer manufacture, process, pack, label and hold various articles of medicated animal feed premixes and non-medicated animal feed mixtures, which premixes and mixtures are held for sale after shipment of certain of their components in interstate commerce; that United Feeds, Inc., and its officers, own the drugs used to prepare such premixes, maintain certain required records governing the manufacture of such premixes, and have been distributing such premixes and feed mixtures; that when shipped and while held for sale after shipment in interstate commerce, the circumstances used in the manufacture, processing, packing and holding of such premixes failed to conform with current good manufacturing practice, and the circumstances of the preparation, packing and holding of the non-medicated animal feed mixtures were under conditions whereby the mixtures might have become contaminated and might have been rendered injurious to health due to contamination with medicated premixes; that FDA inspection of the Wallace Grain Co., Inc., plant disclosed a number of specified deviations from current good manufacturing practice; that FDA analyses of two premixes revealed that they were contaminated with sulfamethazine; that FDA analysis of a "non-medicated" feed mixture revealed the presence, as contaminants, of sulfamethazine as well as the antibiotic Lincomycin; that private laboratory analysis of a "non-medicated" feed mixture revealed sulfamethazine contamination; that when shipped and while held for sale, certain medicated premixes fell below such animal drugs' purported purity and quality; that certain non-medicated feed mixtures contained a non-conforming new animal drug; and that the defendants were well aware that their activities were in violation of the law; 501(a)(2)(B), 501(c), 402(a)(2)(D), 402(a)(4).

A consent decree of injunction enjoined the complained of violations. Three subsequent FDA inspections found the operations to be in compliance. The defendants petitioned for dismissal of the injunction; and, ultimately, the injunction was dismissed. (Inj. No. 833; S. No. 78–120–194 et al.; N.J. No. 27)

Yoshida Dental (U.S.A.) Corp., and **Fumiaki Haga,** vice president and secretary, Hawthorne, C. Dist. Calif.
Charged 10–4–79 in a complaint for injunction: that the defendants had been engaged in importing and selling diagnostic X-ray systems and their major components, until late in 1978; that the defendants had imported and sold several Pampas-E (type 7408) dental units that failed to comply with performance standard regulations as follows: (a) adjustment of the tube head support arm to its lowest position could crush the power supply cable resulting in continuous unintentional radiation emission; (b) the deviation of tube current and exposure time technique factors exceeded the limits specified in the user information; (c) the radiation exposure timers were inaccurate at setting of .1 second; (d) the user information failed to include a description of the measurement basis upon which the exposure time, peak tube potential, tube current, and/or other technique factors were stated; and (e) labels on each unit failed to include a full four-digit year of product manufacture; that FDA had informed the defendants that such defects and failures presented a potential health hazard and had instructed the defendants to repair the dental units and to warn the owners of the dental units; that the defendants' corrective action plan provided for correction by April 1, 1977; that the projected completion date had been extended four times (the last time April 30, 1979); that the defendants had not completed their corrective action plan; that FDA inspections since January 1979 revealed that more than 50 percent of the dental units had either not been corrected at all or had not been corrected adequately or in conformance with the corrective action plan; that a number of specified units had been found to be deficient and/or defective; that FDA inspections revealed that, in a number of cases, the defendants had compounded the violations by performing "corrections" improperly; and that the defendants had been advised and warned concerning the alleged violations and failure to correct deficiencies; 42 U.S.C. 263(j)(a)(1) and (2). The government's complaint for injunction also sought civil penalties (see N.J. No. 19 of this issue of FDA CONSUMER).

A consent decree of permanent injunction enjoined the defendants from: (a) introducing, or delivering for introduction into interstate commerce, any diagnostic X-ray system subject to but not in compliance with prescribed performance standards, and (b) failing to make any required report, to furnish or preserve required information or to permit required entry or inspection. The defendants were further required to bring each of their dental X-ray units into conformity with the applicable standards by: (a) employing qualified and competent technicians to implement corrections to all X-ray units; (b) making all necessary corrections in conformity with the FDA approved written corrective action plan and supplement; (c) inspecting and bringing into compliance, within 90 days, all X-ray units distributed or sold by them whose location was currently known; (d) locate within 30 days the purchaser of each X-ray unit, make all reasonable attempts to locate the X-ray units, and report the location to FDA; (e) inspect and bring into compliance each of defendants' dental X-ray units within 90 days of the unit's discovery; and (f) notify FDA when all corrections have been completed and every 30 days submit progress reports to FDA until the completion of all corrections. The decree also provided for the payment of civil penalties. (Inj. No. 911; S. No. 79-140-286 et al.; N.J. No. 28)

NOTICES OF JUDGMENT on Miscellaneous Action

Statements in an affidavit and deposition by FDA employee, and **suit for damages,** at Montgomery, M. Dist. Ala.

Charged 6-8-79 by H. Ray Evers, M.D., sole proprietor of Ra-Mar Clinic, Montgomery, Ala., against FDA District Director George R. White, Atlanta, Ga., et al., in a suit for exemplary and punitive damages: that George R. White signed an affidavit for the purpose of filing a civil lawsuit and gave a deposition in conjunction with the civil lawsuit on behalf of FDA in which the plaintiff's professional reputation was impugned and maligned, that the plaintiff had made a written demand for a retraction and no retraction had been published.

The government moved to dismiss the action on the basis that the complaint failed to state a claim upon which relief could be granted, that the defendent had not been properly served with process, or, in the alternative, that the court grant summary judgment on the ground that the statements were made while George R. White was engaged in the performance of his official duties and were within the line and scope of his official authority.

Upon submission of the cause to the court on George R. White's motion for summary judgment, the court was of the opinion that there were no material issues of fact and that the defendant was entitled to judgment as a matter of law. In the court's memorandum opinion, the court said:

FACTS

"The pleadings, affidavits and exhibits submitted to this Court disclose the following material facts.

"1. Defendant White is, and was at all times pertinent to this suit, the Director of the Atlanta District, Region IV, of the Food and Drug Administration.

"2. Mr. White's duties include the supervision and enforcement of laws and regulations relating to the production, use, storage and consumption of drugs, food and cosmetics. Defendant White's geographical area of responsibility includes Alabama, Georgia, North Carolina and South Carolina.

"3. In his capacity as District Director, Defendant White became aware of legal action against the Plaintiff in September, 1976, in the Eastern District of Louisiana (C.A. 75-1970) in which the Plaintiff was ordered to discontinue the administration of chelating drugs due to his promotion for other than their intended and approved use.

"4. Upon finding out that the Plaintiff had moved his practice to Montgomery, Alabama, Defendant White directed that an investigation be instituted to determine whether the Plaintiff was continuing the unauthorized use of chelating drugs in his new location.

"5. Upon finding considerable evidence that the Plaintiff was promoting and administering chelating drugs for unauthorized uses, Defendant White recommended to the Food and Drug General Counsel that legal action be considered to enjoin the Plaintiff from such promotion and administration. As Atlanta District Director, Defendant White submitted an affidavit which was filed in support of a complaint for injunction. (M.D. Ala., Civil Action No. 78-93-N.)

"6. In that affidavit, the Defendant White referred to the Louisana case and stated that there was evidence in that case showing that the deaths of at least 14 persons were caused by the Plaintiff's use of Disodium Edetate in treating arteriosclerosis and related diseases. Defendant White affirmed this statement in a deposition given on June 2, 1978, in conjunction with Civil Action No. 78-93-N.

"7. Defendant White's statements relating to 'the deaths of at least 14 persons' were based upon evidence received and considered by Judge Gordon in *United States* v. *An Article of Drug-Diso-Tate, etc., H. Ray Evers, et al.*, ¶ 38,086 FDC Law Reports (E.D. La., C.A. 75-1790, d. Sept. 28, 1976). This evidence was in the form of testimony given by Dr. John David Spence, a qualified expert in internal medicine.

CONCLUSIONS OF LAW

"Federal officers and employees of the executive branch are clothed with absolute immunity from libel suits resulting from oral or written statements made 'within the outer perimeter' of the employee's line of duty. *Barr* v. *Matteo*, 360 U.S. 564, 575 (1959). This Court is of the opinion that Defendant White's acts, as stated in the facts above, were clearly within his line of duty and employment. This point has not been contested by the Plaintiff, who offered nothing in opposition to the aforesaid motion for summary judgment."

In accordance with the court's opinion, the motion for summary judgment was granted, and the action was dismissed with costs taxed against the plaintiff. (Misc. No. 551; N.J. No. 29)

Notices of Judgment are given pursuant to section 705 of the Federal Food, Drug, and Cosmetic Act. Notices of Judgment report cases involving seizure proceedings, criminal proceedings, and injunction proceedings. Seizure proceedings are civil actions taken against *goods* alleged to be in violation, and criminal and injunction proceedings are against *firms* or *individuals* charged to be responsible for violations. The cases generally involve foods, drugs, devices, or cosmetics which were alleged to be adulterated or misbranded or otherwise violative of the law when introduced into and while in interstate commerce, or while held for sale after shipment in interstate commerce.

Notices of Judgment are prepared by Food and Drug Division, Office of the General Counsel, HHS.

Published by direction of the Secretary of Health and Human Services.

Arthur Hull Hayes Jr., M.D., *Commissioner of Food and Drugs*
Washington, D.C., December 1, 1981

1981 FDA Consumer Index

This is an index of FDA Consumer articles for 1981. It is for use along with the magazine's cumulative index for the years 1967 through 1980. That index goes back to the first issue of the magazine when it was known as FDA Papers. For free copies of the 1967-80 index, write to:

Editor, FDA Consumer
FDA, HFI-20
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Rockville, Md. 20857

These sections, except for GENERAL, represent the major classes of products regulated by FDA. In the GENERAL section are articles that describe FDA programs, policies, functions and responsibilities in general; articles that treat two or more major classes of products; and articles concerning hazardous household substances (now regulated by another agency).

The FOODS section includes all articles concerning food for humans as well as food or feed for animals; also all articles on the subject of pesticides, which are primarily of concern to FDA because of their occurrence as residues in foods.

The DRUGS (HUMAN) section includes all articles about drugs for humans, including biological drugs.

The DRUGS (ANIMAL) section includes articles about drugs for animals, including medicated feeds.

The COSMETICS section includes all articles about cosmetics.

The MEDICAL DEVICES section covers all articles about devices used in medical applications, including diagnostic products.

The RAY-EMITTING PRODUCTS section includes all articles about products that emit rays which have the potential for harm to health, such as X-ray machines, television sets, microwave ovens, sunlamps and mercury lamps.

In the major index sections, subject headings are arranged alphabetically in boldface type. Under these headings the articles are listed chronologically in lightface type by title, month and year of issue, and number of the page on which the article begins, with the most recent articles listed last. The month, year and page number are printed in italics.

Cross references are used in subject headings to minimize duplicate listings and to inform the reader about other articles significantly related to the particular subject. Some articles, though general in nature, may also discuss particular products or product classes, and thus may be listed in both the GENERAL and one or more of the product class sections. A reader seeking information in one of the product sections may sometimes find additional information in articles listed in the GENERAL section on that subject. All cross references are to subjects in the same section unless the name of another index section is included in the reference.

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Roger W. Miller
Editor

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Jimmy Washington has a good chance of having a stroke as early as his dad.

When you're nine, things like strokes aren't supposed to happen to your dad. But they do. Fact is, men have strokes earlier than women, and blacks have a greater chance of suffering a stroke — and a more severe stroke — than whites. Jimmy's own future depends a lot on us.

The American Heart Association is fighting to reduce early death and disability from heart disease and stroke with research, professional and public education, and community service programs.

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You can help us support research and education by sending your dollars today to your local Heart Association, listed in your telephone directory.

American Heart Association

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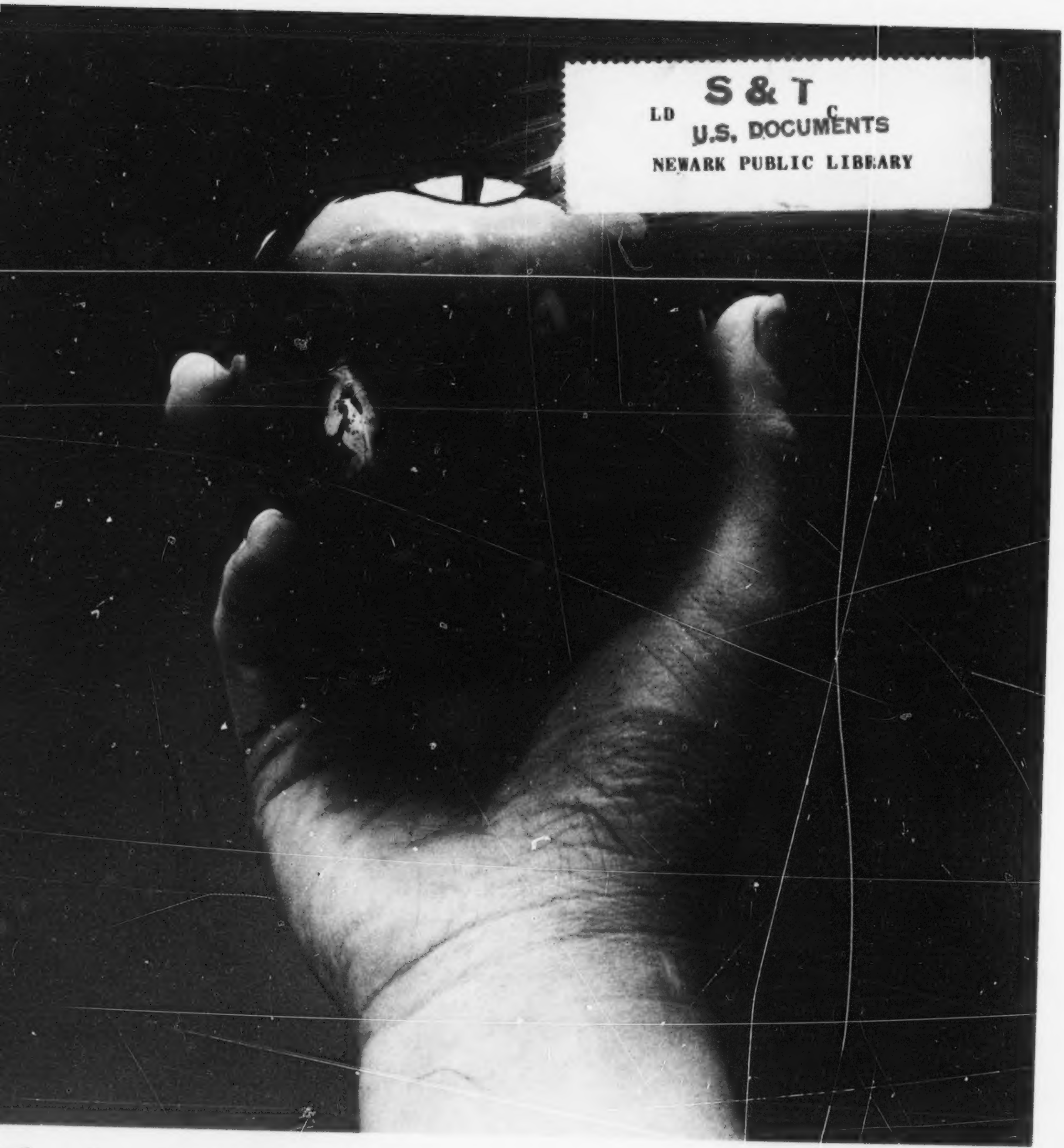

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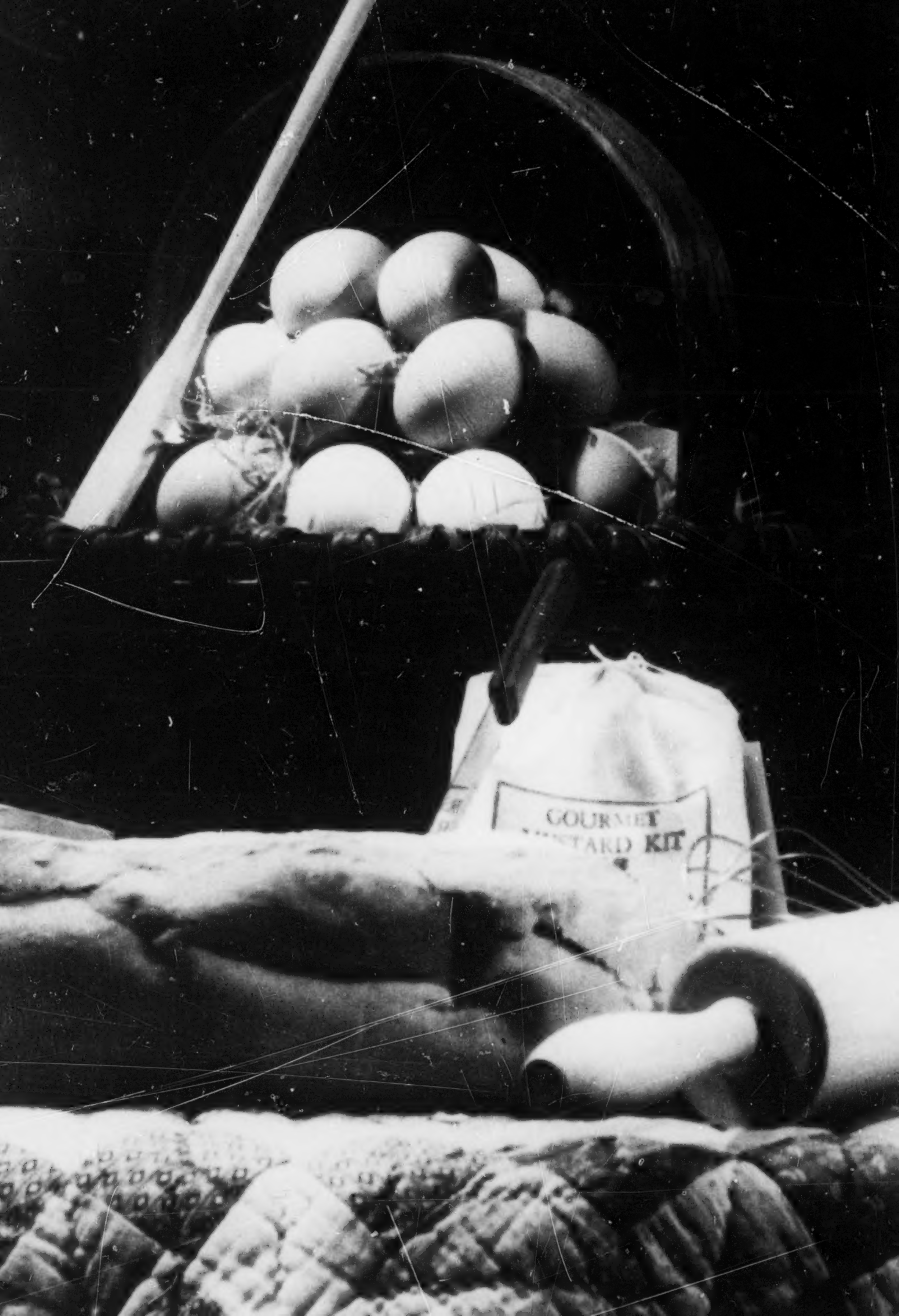
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FDA CONSUMER

VOL. 16 NO. 1 **FEBRUARY 1982**

A Spoonful of Sugar or Sodium Often Goes Down With the Medicine 5
A number of over-the-counter drugs have sugar or sodium among their ingredients. In some cases, the agent is there as an active ingredient. Those who must watch their sugar or salt intake should be cognizant of these items.

How To Shine an Apple 8
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Prostaglandins Are Regulators Extraordinary 12
They are involved in response of tissues to stimuli and injury; they affect blood pressure; they are essential to blood clotting. And science is beginning to find other uses for prostaglandins.

All You Knead To Know About Bread 16
Bread has been called mankind's first fast food. How bread got that reputation and how bread is made today are discussed in this article.

X-rays for Childbirth: Risky, Costly, Not Always Helpful 20
One study indicates that 6 percent of the births in this country are preceded by pelvimetry, i.e., X-raying for size of the baby's head and the mother's birth canal. Not all the pelvimetry being done is necessary and this poses some problems.

The Tanning Pill, a Questionable Inside Dye Job 23
Taking tanning pills sounds like a slick alternative to lying in the hot sun. But the ingredients in the pills haven't been proved safe in the quantities needed to tan from the inside out.

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If it weren't for a giveaway such as the writing on the bag behind the loaf, this picture might have been made in almost any household, anywhere, for bread is important in the diets of practically everybody on our globe. For some basics on the stuff of life, see* All You Knead To Know About Bread, *starting page 16.

Richard S. Schweiker
Secretary, U.S. Department of Health and Human Services

Arthur Hull Hayes Jr., M.D.
Commissioner of Food and Drugs

Wayne L. Pines
Associate Commissioner for Public Affairs

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Section 705 [375] of the Food, Drug, and Cosmetic Act:
(a) The Secretary shall cause to be published from time to time reports summarizing all judgments, decrees, and court orders which have been rendered under this Act, including the nature of charge and the disposition thereof.
(b) The Secretary may also cause to be disseminated information regarding food, drugs, devices, or cosmetics in situations involving, in the opinion of the Secretary, imminent danger to health, or gross deception of the consumer. Nothing in this section shall be construed to prohibit the Secretary from collecting, reporting, and illustrating the results of the investigations of the Department.

Cover Photo: John Troha/Black Star

Updates

Hepatitis Vaccine OK'd

Heptavax-B, a new virus vaccine to combat hepatitis B, a debilitating liver disease, was approved by FDA Nov. 16, 1981. This is the first completely new viral vaccine in 10 years and the first vaccine ever licensed in the United States that is made directly from human blood.

This major advance was brought about by the cooperative effort of scientists in government, industry and the academic community. How it all came about was described in the article "New Vaccine Promises Hepatitis B Protection" in the May 1981 issue of *FDA Consumer*.

Although the vaccine is very important, it is not for general, population-wide use, Commissioner Arthur Hull Hayes Jr. pointed out when he announced the vaccine's approval. It will be recommended initially only for people at high risk of acquiring the disease, such as health care workers, institutionalized mentally handicapped patients, laboratory workers, hemodialysis staff workers and patients, contacts of certain carriers, some military personnel and persons who make numerous sex contacts.

Because of the very lengthy production time, the vaccine will not be available for broad distribution until mid-1982. Cost for the three shots needed for protection is estimated to be between $75 and $120. Heptavax-B is manufactured by Merck Sharp & Dohme of West Point, Pa.

Drug Approved for Heart

Timolol, a drug used primarily as eye drops for the treatment of glaucoma, has been approved by FDA for use in preventing death and further heart attacks among people who have just survived an initial heart attack. Announcement of the approved new use for timolol was made by Commissioner Arthur Hull Hayes Jr. on Nov. 25, 1981.

The approval of timolol was based on a three-year Norwegian study begun in 1978 and conducted in 20 clinical centers serving a third of Norway's population. The study showed that when timolol treatment was begun soon (seven to 28 days) after an initial heart attack, and continued for up to 33 months, the risk of death was reduced by about a third, and the risk of a second, nonfatal heart attack also was reduced by about a third. The study was described in a report published in the April 1981 *New England Journal of Medicine*.

Timolol belongs to a class of drugs known as beta blockers. Another beta blocker, propranolol, was recently reported to have a similar effect in a study by the National Heart, Lung and Blood Institute. In Sweden a study indicates significant reductions in mortality with another beta blocker, metroprolol.

The development of beta blockers began in the early 1960s. FDA approved propranolol in 1967 to treat heart arrhythmias (irregular beats). In 1973 it was approved to treat angina, in 1976 to treat high blood pressure and in 1979 to treat migraine headaches. Timolol eye drops were approved in 1978.

"While these drugs have had wide use in the past decade and a half, their new use holds out great hope for people with heart disease," Commissioner Hayes said. "I am pleased that the United States is one of the first countries to approve timolol for this new use by heart attack patients to prevent deaths and second heart attacks."

Dr. Hayes also announced approval of timolol for treatment of high blood pressure. Timolol as a glaucoma drug was discussed in "Keeping an Eye on Glaucoma" in the June 1980 *FDA Consumer*; beta blockers and other drugs used to treat diseases of the heart were the subject of "Drugs Are Dear to Many Hearts" in the December 1981-January 1982 *FDA Consumer*.

Sugar Consumption Declines

Americans consumed an average of almost 80 pounds of refined sugar each in candies, soft drinks and other foods last year—the lowest amount since 1946. Per capita consumption in that year was just 75 pounds, according to a U.S. agriculture department sugar and sweeteners report issued in December 1981. Per capita sugar consumption had topped more than 100 pounds in the years 1969 through '73.

From 1974 through 1978 consumption remained more than 90 pounds a person. Consumption fell to 89.3 pounds per person in 1979 and 83.7 pounds in 1980.

Americans still have a sweet tooth, the USDA report said, but they are getting part of their sweets from an alternative source: sweeteners produced from corn. USDA predicted a further decline in refined sugar consumption this year reflecting a continuing increase in the use of high-fructose corn syrup, a corn-derived sweetener.

The many facets of sugar were explored in a three-part series of articles in the 1980 volume of

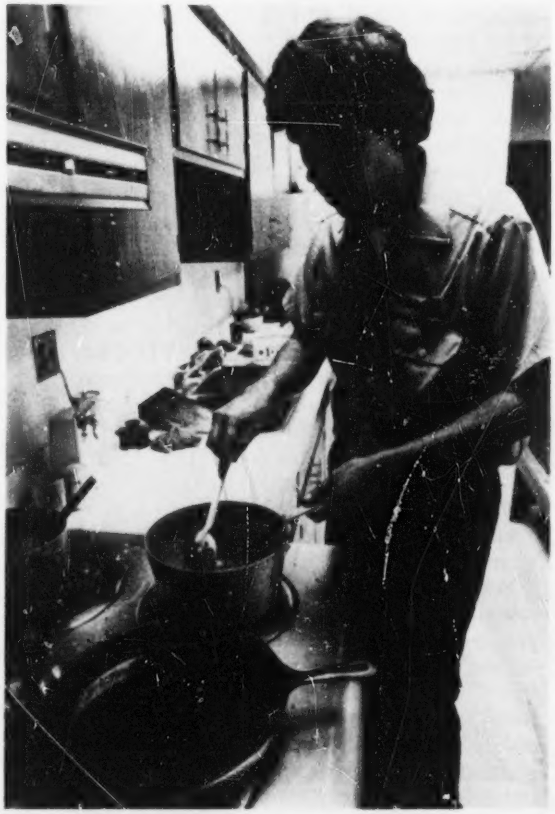
FDA Consumer: "Sugar: How Sweet It Is—And Isn't" in February; "Fructose: Questionable Diet Aid" in March; and "Food Labels and the Sugar Recognition Factor" in April.

Fireman Praised

A nationwide recall of canned mushrooms last year was set off by a Rockford, Ill., fireman, Ron Hill, and was recounted in the October 1981 issue of *FDA Consumer* in an article titled, "1 Alert Cook + 1 Bad Can of Mushrooms = A Total Recall." One of the magazine's readers, Tim Kostka, a pharmacist who lives in Woodridge, Ill., found Hill's efforts worthy of a letter. The letter is reprinted here with Mr. Kostka's permission.

Dear Ron:

I have been working in an FDA regulated industry for several years now. As you can imagine there is quite a volume of newsletters, journals, and magazines that I must read to stay abreast of all the regulations. As I was sorting through this sometimes boring and tedious material one day, I came upon a botulism recall article in the *FDA Consumer* magazine. The article left me with such a good feeling, I wanted you to know that I appreciated the action you took. As long as I have been in the health field I can't remember saving someone's life. It seems as if the FDA has received most of the credit, but your part was crucial too.



As soon as I heard of the recall, my wife and I returned all of our canned mushrooms to the store. Soon after that, I heard that a Rockford fireman initiated this massive FDA recall. I didn't know until now who that person was.

The Food and Drug Administration has been criticized for many years as an over regulating, bureaucratic organization. I have always contended that the FDA is necessary and worthwhile. . . . This incident proves that point.

It's nice to know that one person can still accomplish a great deal by taking positive action.

Many people would not have made that phone call for fear of getting involved and wasting their time. Concerned individuals like yourself are a rare commodity; I just hope other people follow your example.

So I'd like to thank you not only on behalf of myself and any people you may have saved from botulism, but on behalf of FDA regulated medical industry as well.

Tim Kostka, R.Ph.
Woodridge, Ill.

Antibiotic Certification To End

FDA has notified its employees that it plans to propose a change in its regulations that would phase out its antibiotics batch certification program by next October.

Under this program the agency has checked the purity and potency of every batch of antibiotics produced by manufacturers for 35 years. All manufacturers have been required to have their products certified before distribution.

The program began in 1945 when antibiotics were new and the technology for their production could not be depended on to assure their potency, purity and quality. Today, however, manufacturing quality control and standards for antibiotics are comparable to those for other drugs.

Thus, in a first step toward reducing the program, FDA last year exempted from certification a small category of topical antibiotics for skin and vaginal infections. A similar proposal to exempt antibiotic preparations for the ear and eye is nearing completion within the agency.

At the same time, Vice President George Bush's Task Force on Regulatory Reform and FDA itself (following the agency's request in the *Federal Register* for candidates for regulatory review) have received comments that the program is no longer necessary in view of the high level of quality control in the industry and the low rate of batches rejected by the antibiotic certification program (less than 1 percent). The General Accounting Office recently concluded that FDA should reduce the level of testing of antibiotics.

The phase-out will leave antibiotics subject to the same regulatory controls as other drugs, including review and approval of applications, inspections and surveillance of products in the marketplace.

The program, which has employed 190 people, has been financed by industry fees so the impact of the change on the federal budget will be small. However, industry and the economy will be spared unnecessary costs and warehouse time. The agency will maintain a residual analytical capability for antibiotics consistent with the resource level devoted to other drugs.

During fiscal year 1981, fees totaled $6,084,751, and 18,819 batches of antibiotics were certified.

Court Backs Color Review

The U.S. District Court for the District of Columbia has upheld FDA's decision to give industry more time to complete safety reviews of 23 color additives used in foods, drugs and cosmetics. The colors are on the agency's provisional list, permitting their use until safety tests determine whether they are to be "permanently" approved or withdrawn from the market.

The Public Citizen, a consumer group, had challenged FDA's rule to extend the provisional listings, holding that the closing dates for the tests had already expired, and that it was necessary to expedite the testing and review process "to assure the public's safety as soon as possible."

In deciding against Public Citizen's motion to ban the provisionally listed colors, Federal Judge Thomas A. Flannery held that under the law the FDA commissioner is required only "to ensure that testing is completed 'as soon as reasonably practicable.' In this case the Commissioner clearly found both that there were reasons for the delays that had occurred and that there was good reason for allowing the present extensions."

Under the extended schedule, 12 of the 23 color additives will have closing dates in 1982, nine in 1983 and two in 1984. Why and how FDA regulates color additives was explained in "The Color Additive Scoreboard" in the March 1980 *FDA Consumer*.

Expense Recovery Denied

FDA's "pilot" program under which certain participants in agency proceedings could recoup their expenses has been ruled invalid by a federal appeals court. The majority of the three judges at Richmond, Va., held in their November ruling that only reimbursement programs specifically enacted by Congress are legal.

The reimbursement program, established in 1979, was to provide funds to cover the expense of reasonable attorneys' fees, expert witnesses, clerical services, travel, studies, demonstrations and other reasonable and necessary costs incurred by certain qualified individuals or organizations participating in agency rule-making proceedings who would not otherwise be able to participate. The agency had earmarked $250,000 for the program. (How one woman made use of these funds is part of the story in "How Consumers Get Activated" in the November 1980 *FDA Consumer*.)

The legality of the program was challenged in the U.S. District Court for the District of Maryland by the Pacific Legal Foundation, which had participated in FDA proceedings at its own expense. The district court held that FDA had the authority to establish the reimbursement program. The foundation appealed.

FDA now has the option of requesting a hearing before the entire appeals court (U.S. Court of Appeals for the Fourth Circuit) or taking the case to the Supreme Court. Until a decision is made, no funds will be available for the reimbursement program.

While a number of agencies do have congressional authorization for similar reimbursement programs—i.e., the Environmental Protection Agency, the Federal Trade Commission, the Consumer Product Safety Commission and the Federal Energy Regulatory Commission—FDA, the Department of Agriculture and the Federal Deposit Insurance Corp. have set up such programs without specific authority from Congress.

A Spoonful Of Sugar Or Sodium Often Goes Down With The Medicine

by John M. Couric

People trying to avoid high sugar or sodium intake have to watch more than what they eat. Many drugs contain sugar or sodium in various amounts, and it's often up to the consumer to keep up with how much he's getting from these other sources, particularly if over-the-counter (OTC) drugs are taken that the doctor doesn't know about.

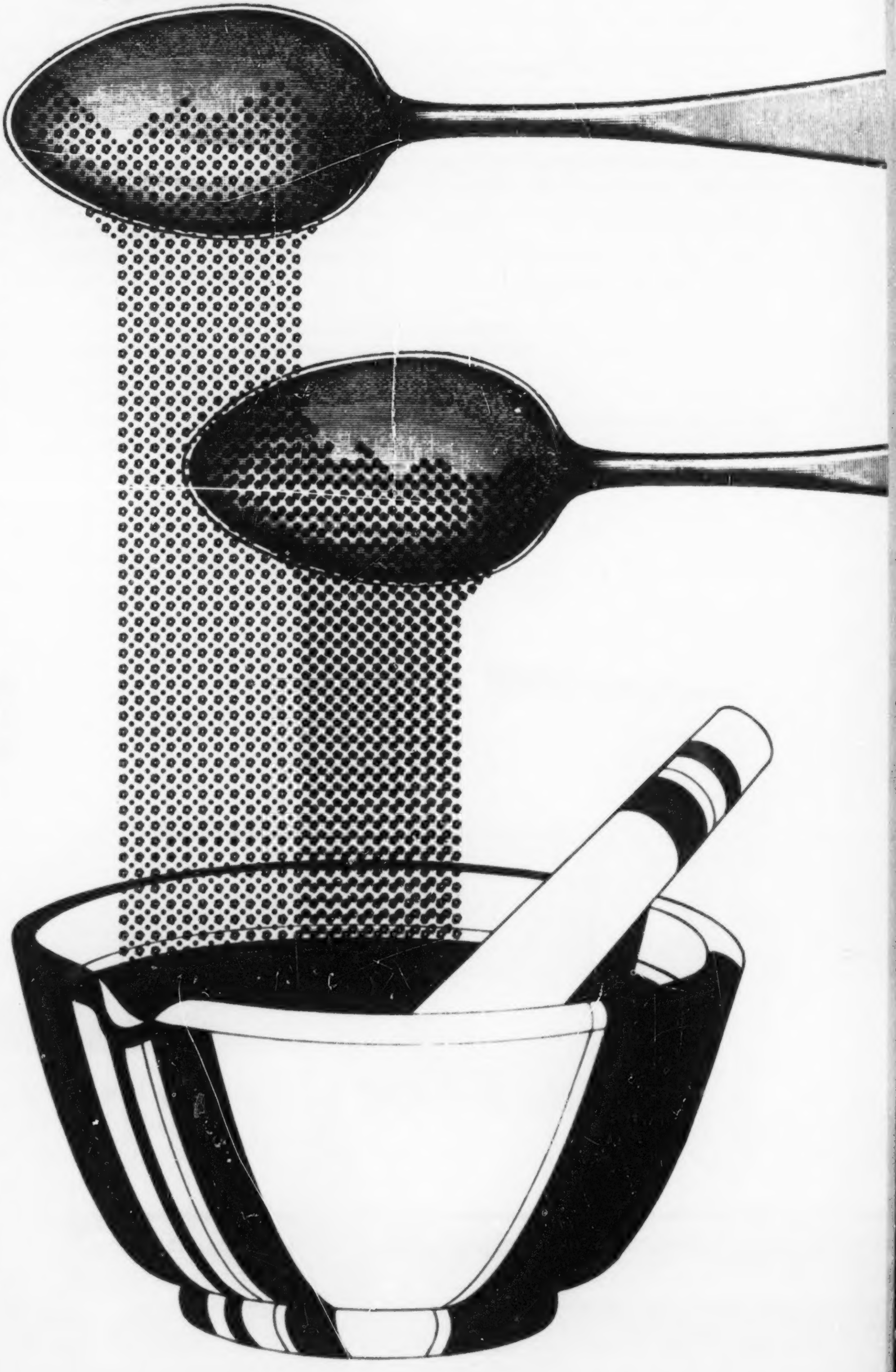
Sugar, of course, is a no-no for diabetics, and cutting down on sugar is also an important way to control calorie intake to keep body weight down. But for healthy people who can maintain normal weight, eating lots of sweets hasn't been found detrimental except possibly in causing tooth decay.

The bugbear of excess sodium is high blood pressure—called hypertension. Reducing sodium intake is usually one way to keep blood pressure down to acceptable levels. Taking in too much sodium makes hypertension worse and also is believed to be a factor in causing that disease (although heredity may be the most important factor in the body's sensitivity to sodium's effect on blood pressure). Societies that don't get much sodium in their food have a much lower incidence of hypertension.

People can't avoid sodium altogether because it's part of the normal chemical composition of many foods. Furthermore, it is impossible to survive without sodium in the diet. It helps attract water into the blood vessels, thus maintaining proper blood volume and generally constant pressure. Sodium also helps produce hormones that regulate blood pressure, and it assists in adjusting the body's acid-alkaline balance.

Sugar is used in many OTC drugs to give viscosity and consistency to fluids and to improve palatability. The sodium compounds used in OTC drugs are active ingredients.

Currently, the medical profession is not able to identify persons who



are particularly sodium sensitive and thus likely to develop hypertension. Nevertheless, it is reasonable for everybody to cut down on sodium. The Food and Nutrition Board of the National Academy of Sciences-National Research Council says intakes of 1,100 to 3,300 milligrams (mg) of sodium per day are adequate and safe for a healthy adult. That much—and more—comes from consumption of ordinary table salt, which is 40 percent sodium and 60 percent chloride. One teaspoon of salt equals about 2,000 mg of sodium. Americans consume about 1 to 3 teaspoons of salt each day, or between 2,000 and 6,000 mg of sodium.

Of the OTC drugs, antacids and analgesic/antacids are particularly likely to contain sodium, according to the United States Department of Agriculture publication *The Sodium Content of Your Food.* That publication includes an American Medical Association table showing the sodium content of selected non-prescription drugs. This USDA publication may be ordered through the Food and Drug Administration.

The various brands of analgesics containing aspirin are at the low end of the table with 49 mg of sodium per dose. At the upper end, the antacid laxative Sal Hepatica, which contains sodium bicarbonate, sodium monhydrogen phosphate and sodium citrate as ingredients has 1,000 mg of sodium per dose.

Here's the score on some selected antacids: Rolaids (containing dihydroxy aluminum and sodium carbonate) 53 mg per dose; Soda Mint (sodium bicarbonate) 89 mg; Alka-Seltzer Antacid (in the gold box) (sodium bicarbonate, potassium bicarbonate and citric acid) 276 mg; Brioschi (sodium bicarbonate, tartaric acid and sucrose) 710 mg.

The antacid analgesic Bromo-Seltzer, which has acetaminophen and sodium citrate as ingredients, contains 717 mg of sodium per dose; Alka-Seltzer in the blue box, containing aspirin and sodium citrate, has 551 mg of sodium per dose. Sleep-aids are not exempt. Miles Nervine Effervescent with its sodium citrate contains 554 mg of sodium per dose.

In the laxative category, Metamucil Instant Mix, containing psyllium, sodium bicarbonate and citric acid, has 250 mg of sodium per dose; and Fleet's Enema, with sodium biphosphate and sodium phosphate, contains 250 to 300 mg of sodium which the body absorbs per dose.

Because the specified doses vary for the antacid suspension products, the AMA has chosen to give sodium content in milligrams per 100 milliliters of the product instead of the dose so that the consumer can tell how much sodium is in a bottle of a certain size (in milliliters). Milk of Magnesia with its magnesium hydroxide has 10 mg per 100 ml. The others: Amphogel (aluminum hydroxide) 14 mg; Basalgel (aluminum carbonate) 36 mg; Maalox (magnesium hydroxide and aluminum carbonate) 50 mg; Riopan (magnesium aluminum complex) 14 mg; Mylanta I (magnesium hydroxide) 76 mg; Mylanta II (aluminum hydroxide) 160 mg; Di-Gel(simethicone)170 mg; and Titralac (calcium carbonate) 220 mg.

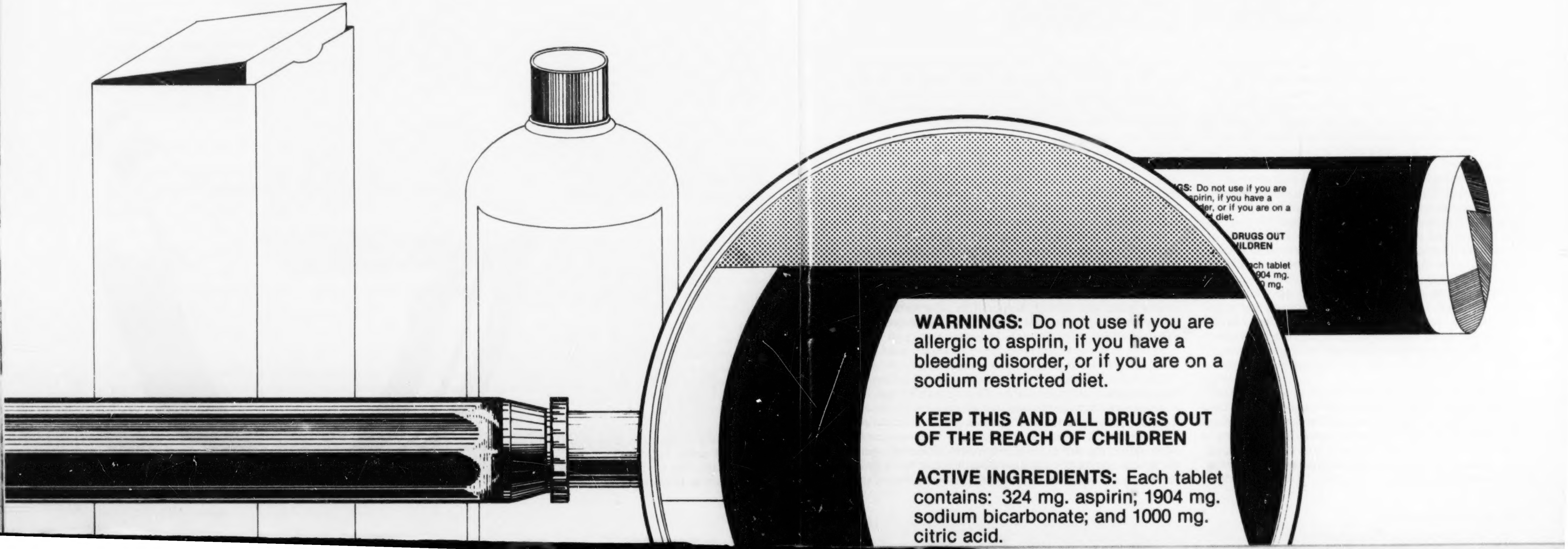
Some antacids not only contain significant amounts of sodium but sugar or saccharin as well. Writing in *The New England Journal of Medicine,* David C. Stolinsky, M.D., of the University of Southern California School of Medicine, points out that these are so-called "inactive" ingredients that FDA does not require to be listed on the label. Nor are they always listed in the *Physicians' Desk Reference* or other standard sources, he notes.

The American Diabetes Association, recognizing that long use of these antacids could interfere with control of diabetes, distributes a list of sugar-free liquid preparations including but not limited to antacids. The list was compiled by *American Druggist* magazine, which declared: "Sugar-free medications to treat these severe conditions (diabetes mellitus and its accompanying diseases) are vital. A more subtle danger arises, however, when diabetic patients attempt to self-medicate for what they may regard as a minor affliction: 'heartburn,' diarrhea, cough and fever of a cold, constipation. Many OTC products [used] to treat the conditions have hidden sugar used as diluents, binders, fillers, flavoring and coloring agents, and sweeteners. At this time, the FDA does not require complete disclosure of these agents. Even if such ingredients are listed, patients may not fully understand their impact on a sugar-restricted diet. Pharmacists can guide patrons in the all-important medication selection."

Sometimes reading the label will tell all one needs to know about the content of an OTC drug. The Alka-Seltzer blue box, for example, says, "Do not use . . . if you are on a sodium restricted diet. Each tablet contains 551 mg of sodium." Similar warnings are voiced on the labels for other upset stomach products such as Gaviscon and Brioschi. The Rolaids package notes that each tablet contains 53 mg of sodium, while Bromo Seltzer advises people on a sodium-restricted diet to consult with their physician before using the product.

Consumers should consult their physician or pharmacist if at all in doubt.

John M. Couric is a writer/editor with FDA's Bureau of Drugs.


WARNINGS: Do not use if you are allergic to aspirin, if you have a bleeding disorder, or if you are on a sodium restricted diet.
KEEP THIS AND ALL DRUGS OUT OF THE REACH OF CHILDREN
ACTIVE INGREDIENTS: Each tablet contains: 324 mg. aspirin; 1904 mg. sodium bicarbonate; and 1000 mg. citric acid.

How To Shine An Apple

by Chris Lecos

They make shoes shiny, floors glossy and cars the glittering envy of the neighborhood. And, one might add, they give a sensual sparkle to a woman's lips. Such are the uses that come to mind for most people when the subject is waxes. What many may not realize is that waxes also give many fruits and vegetables their eye-appealing sheen while neatly stacked in a supermarket's display bin.

There is nothing new about using waxes on produce after harvesting. The Chinese were dipping oranges and lemons in molten waxes—to make the fruit ferment—as early as the 12th or 13th century. American fruit and vegetable packers and processors have been coating many of these perishable products for more than 50 years, according to the United Fresh Fruit and Vegetable Association in Alexandria, Va.

Industry sources and trade publications cite various reasons why waxy coatings are applied to fruits and vegetables after harvesting. One simple reason is that a shiny apple, grapefruit or cucumber, for example, is a lot more attractive to the consumer, and therefore more salable. Waxing also adds a protective coating that helps retard moisture evaporation.

Most fruits and vegetables contain 80 to 95 percent water by weight. They are still "alive" when plucked from a tree, vine or the ground, and the loss of water from living tissue, a process called transpiration, causes weight loss, shriveling and wilting. This, of course, means poorer texture and quality, including loss of vitamins and other nutritional qualities.

Fruits and vegetables, stored under the same conditions, lose water at varying rates. Their protective surface plays a role in this. Leafy vegetables such as celery and lettuce lose water rapidly; apples, melons, squash and others whose surfaces are protected by a smooth or glossy skin lose moisture more slowly.

Many commodities—apples, pears, citrus products generally—have a natural wax covering that varies in thickness. Carrots and turnips have less of a natural wax coat than apples and pears and thus lose moisture more rapidly. A tomato, with its relatively impermeable skin, loses moisture mainly through the stem scar.

During the growing period, produce accumulates dirt and residues from chemical spraying. Many products are cleaned with solvent detergents by packers, which may remove the natural wax covering. This can reduce the market life of many perishables. Washing increases the rate of water loss through evaporation. Also increased is the aerobic respiration rate or inhalation of oxygen and exhalation of carbon dioxide and moisture through the microscopic pores of the products. This causes a decrease in sugar and loss of flavor and of ascorbic acid.

To retard this chain of events, the produce industry relies on sophisticated and highly effective cold storage techniques to slow respiration and extend storage life—for many months in the case of some products, such as apples. For some products, says the U.S. Department of Agriculture, the processes of respiration, ripening, aging, decay and certain physiological disorders can be slowed further by reducing the oxygen level or by increasing the carbon dioxide content of the storage air, or by both, to extend storage and shelf life. So-called controlled-atmosphere storage, a refrigerating method in which oxygen and carbon dioxide levels are controlled and adjusted carefully, is a major means of storage that is used today. But the application of wax or wax emulsion preparations to perishables also is fairly common.

According to USDA, the commercial use of wax preparations is rather extensive on citrus, rutabagas and cucumbers. Their use is more limited on some other crops, including peppers, mature-green tomatoes, cantaloupes, honey dew melons, apples and sweet potatoes. In the case of citrus and root crops, the department says, waxing helps reduce moisture loss and thus retards shriveling. With other products, USDA adds, an improved glossy appearance is the main advantage. Waxing alone does not control decay as is sometimes claimed, but waxing and fungicides combined are sometimes beneficial, USDA says. This means that fungicides, bactericides, growth regulators and substances that inhibit natural aging or ripening may be mixed in with the wax formulations. Even coloring agents are included in some formulations.

A textbook on industrial waxes points out that one of the best grades of Florida oranges—superior to other varieties in juice and vitamin content—is treated with a wax coating to which red or orange color is added because the fruit ripens in its natural state to a russet or greenish color. Appearance, in other words, is the main concern.

Just how extensively wax coatings are used is not clear, although the practice is considered fairly widespread for many products. In 1976 the Center for Science in the Public Interest, a Washington-based consumer advocacy group, complained to the Food and Drug Administration that waxes were being used widely with some commodities and that, in many instances, the products were being sold without the required labeling information on display, thus preventing consumers from knowing that waxes were used on the products.

Through contacts with industry sources, CSPI said that about 35 to 40 percent of the fresh apples, about half the fresh tomatoes and three-fourths of the cucumbers were being treated with wax at domestic packing plants.

The waxes that are used to coat fruits and vegetables or that are components of coatings for produce come under the purview of FDA's food additive regulations. There are many. The regulations usually set limits on how much can be applied to fruits and vegetables and in a number of instances specify the fruits and vegetables to which they can be applied. In some other cases, the additives have general or multiple food uses.

For example, coumarone-indene resin (produced from the crude, heavy, coal-tar solvent naptha) is a food additive that FDA says can be used safely on grapefruit, lemons, limes, oranges, tangelos and tangerines so long as the maximum amount of resin remaining on the fruit does not exceed 200 parts per million on a fresh weight basis. There is a separate regulation that says petroleum naptha can be used as a solvent in protective coatings on fresh citrus fruits. In the case of oxidized polyethylene, the regulation says it can be used as a protective coating or component of protective coatings for fresh avocados, bananas, beets, coconuts, eggplants, garlic, grapefruit, lemons, limes, mangoes, muskmelons, onions, oranges, papayas, peas (in pods), pineapples, plantains, pumpkins, rutabagas, squash, sweet potatoes, tangerines, turnips, watermelons and all nuts in shells. In normal consumption, the outer covering of most of these products is removed along with the polyethylene before they are eaten.

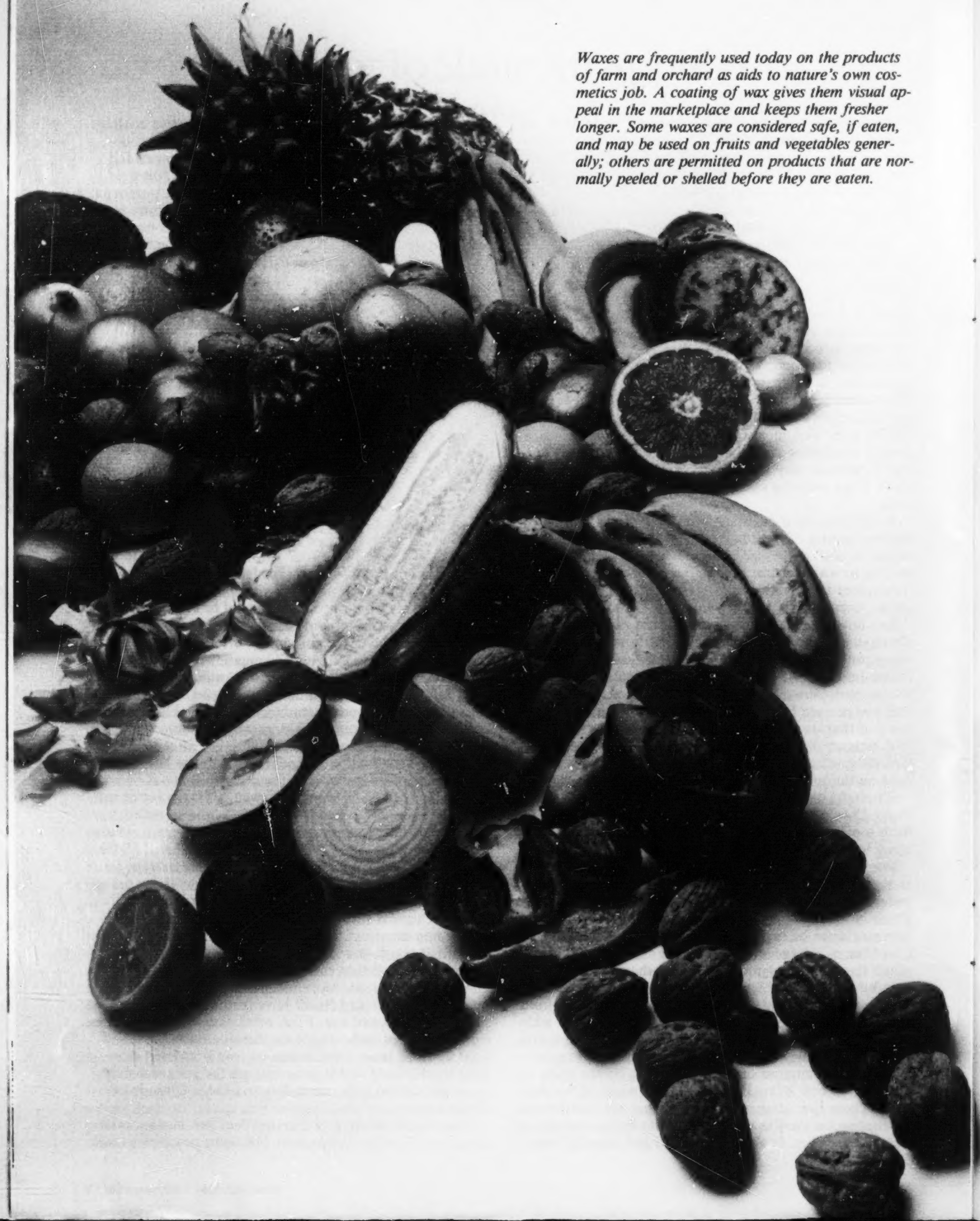
Commercial waxes generally are derived from plant and petroleum sources and usually consist of a combination of shellac, carnauba, polyethylene or paraffin-type waxes that are mixed with water and emulsifying and wetting agents to provide a thin, continuous film of wax on the products. The first resin coating process was developed in 1940. With citrus products, a thin coating of physiologically inert coumarone-indene resin is applied. Waxes are applied to produce in various ways: by brushing, fogging, foaming or, as the produce travels over a conveyor, through a tank of wax emulsion.

Only waxes and wax components that are considered safe and for which FDA has scientific data that demonstrate no public hazard are allowed for use by the agency. The food additive regulations adopted by FDA prescribe the safe conditions for use of the components. As former FDA Commissioner Alexander M. Schmidt noted in his reply to CSPI in 1976: "If we had substantial scientific data demonstrating that these substances or any other food additives would present a hazard to consumers, all necessary measures provided for in the law would be undertaken to protect the consumer."

Under the Food, Drug and Cosmetic Act, which spells out FDA's legislative and regulatory authority, chemicals may not be added to food unless they have been tested for safety by appropriate studies of animals. However, such premarket testing and clearance requirements apply only to those additives that came into use after Congress enacted the food additive amendments to the law in 1958. Many substances in common use prior to that year were at the time placed on what is known as FDA's list of substances "generally recognized as safe"—the so-called GRAS list. For some years now, FDA has been conducting a scientific review of all substances on the GRAS list under a contract to determine whether more current scientific information would affect the present safe status of the additives. This review, by the Federation of American Societies for Experimental Biology, already has covered a number of waxes.

FASEB concluded in a 1975 report that there was no reason to believe that carnauba wax might be unsafe for human consumption. More recent studies commissioned by the government of Brazil have further affirmed its safety for continued use, FDA officials said. Derived from the leaves and buds of the Brazilian wax palm and used in foods since 1900, carnauba wax is not metabolized by the body and it goes through the system mainly in an undigested state, according to FDA's Division of Toxicology.

That it goes through undigested does not mean a consumer would suffer indigestion. It is inert and causes no ill



Waxes are frequently used today on the products of farm and orchard as aids to nature's own cosmetics job. A coating of wax gives them visual appeal in the marketplace and keeps them fresher longer. Some waxes are considered safe, if eaten, and may be used on fruits and vegetables generally; others are permitted on products that are normally peeled or shelled before they are eaten.

effects, and at the levels used, it poses no problems to humans, FDA toxicologists explained. The same is true of paraffin wax. Most of it goes through the system unchanged and introduces no toxicological problems.

In another 1975 report, FASEB noted that it found no evidence to demonstrate that beeswax is a hazard to the public. Its report indicated there is little experimental data on digestion, absorption, metabolism and short- or long-term toxicity of beeswax after oral intake by humans or animals. Beeswax is a secretory product of honeybees collected from plants and is used as structural material in honeycombs. The combs are melted in hot water or steam and strained to remove honey and bee and cocoon fragments. The crude wax obtained then undergoes a refining process. Like carnauba wax, it also has many nonfood uses.

Candelilla wax, used chiefly in food as a component of chewing gum base and as a glaze for hard candies, is a complex substance derived from several species of Euphorbiaceae, a family of plants that grow mainly in semiarid regions of northern Mexico and southern Texas. FASEB last year also reported there was no available evidence to suggest candelilla wax is a hazard to the consuming public.

FDA field investigators check how waxes are used when inspections are made at packing facilities although the agency relies heavily on state and local enforcement agencies to obtain compliance with labeling requirements at the retail level. FDA regulations require labels on foods, including the list of ingredients used, but the law permits exemptions where compliance is "impracticable." Individual labeling of fresh fruits and vegetables falls into the exempt category.

The exemption applies to foods received in bulk containers at retail establishments. In such cases, the labeling information must be displayed to consumers on the bulk container, which must be in plain view, or through the use of a counter card, sign or other appropriate device that prominently and conspicuously bears the required ingredient information. Absence of a proper declaration of ingredients by retail establishments on the sales bin or counters renders the food misbranded under the provisions of the act, according to current FDA policy.

FDA officials point out that enforcement is left primarily to local agencies because the agency lacks manpower and resources to inspect at the thousands of food and other retail stores for possible labeling violations. As Commissioner Schmidt explained to CSPI in 1976: "Because of resource constraints, it is not possible to initiate enforcement action against every infraction of the law, especially misbranding violations in retail outlets throughout the country. We consider labeling violations not involving health hazards to be a low priority for enforcement. To bring enforcement action against them, the agency would have to divert resources from more critical areas, bearing on the microbiological and chemical contamination of foods, drugs and cosmetics and the distribution of inefficacious drugs and devices which threaten the life and health of consumers."

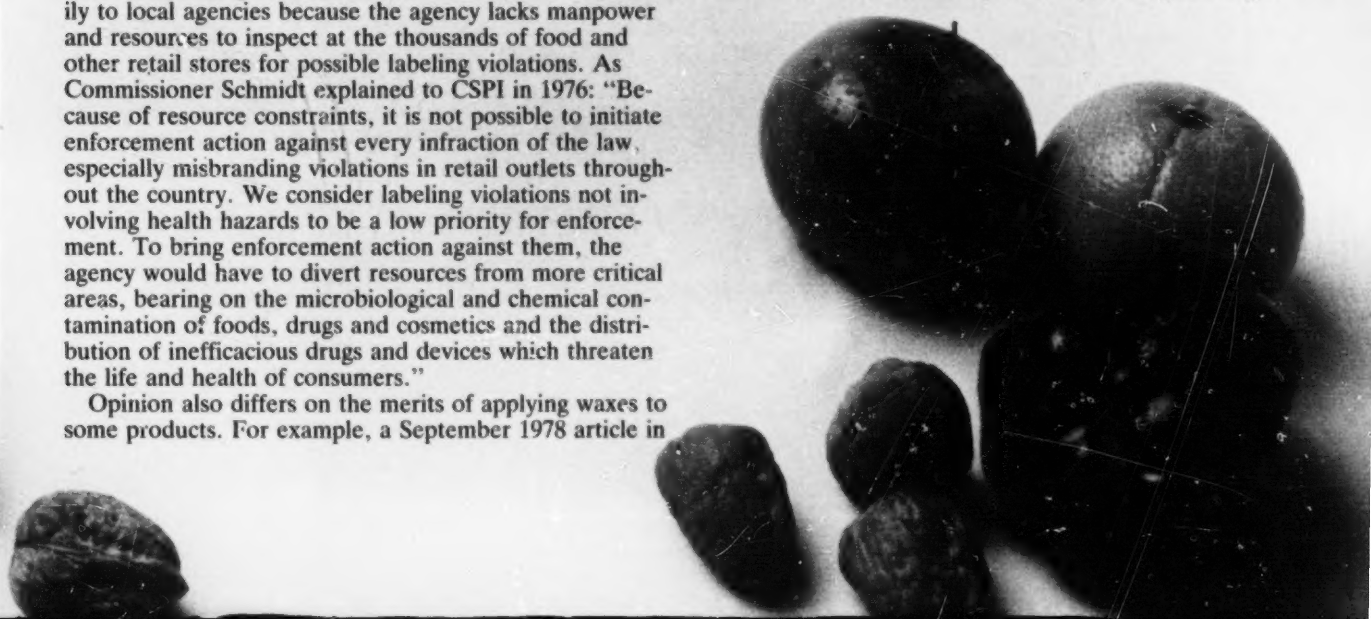
Opinion also differs on the merits of applying waxes to some products. For example, a September 1978 article in *The Packer*, a publication of the fresh fruit and vegetable industry, said the reason for waxing apples is mainly for cosmetic effect. The author, Hans Buttkus, a researcher in the food processing section of Canada's Summerland, British Columbia, Research Station, went on to say: "Shiny, waxed apples sell more readily than unwaxed ones. The industry feels it is required by a competitive market to supply the convenience food-oriented North American public with a clean, ready-to-eat apple. This demand almost seemed to be met by the detergent-washed, carnauba- and shellac-wax-coated apples. . . ."

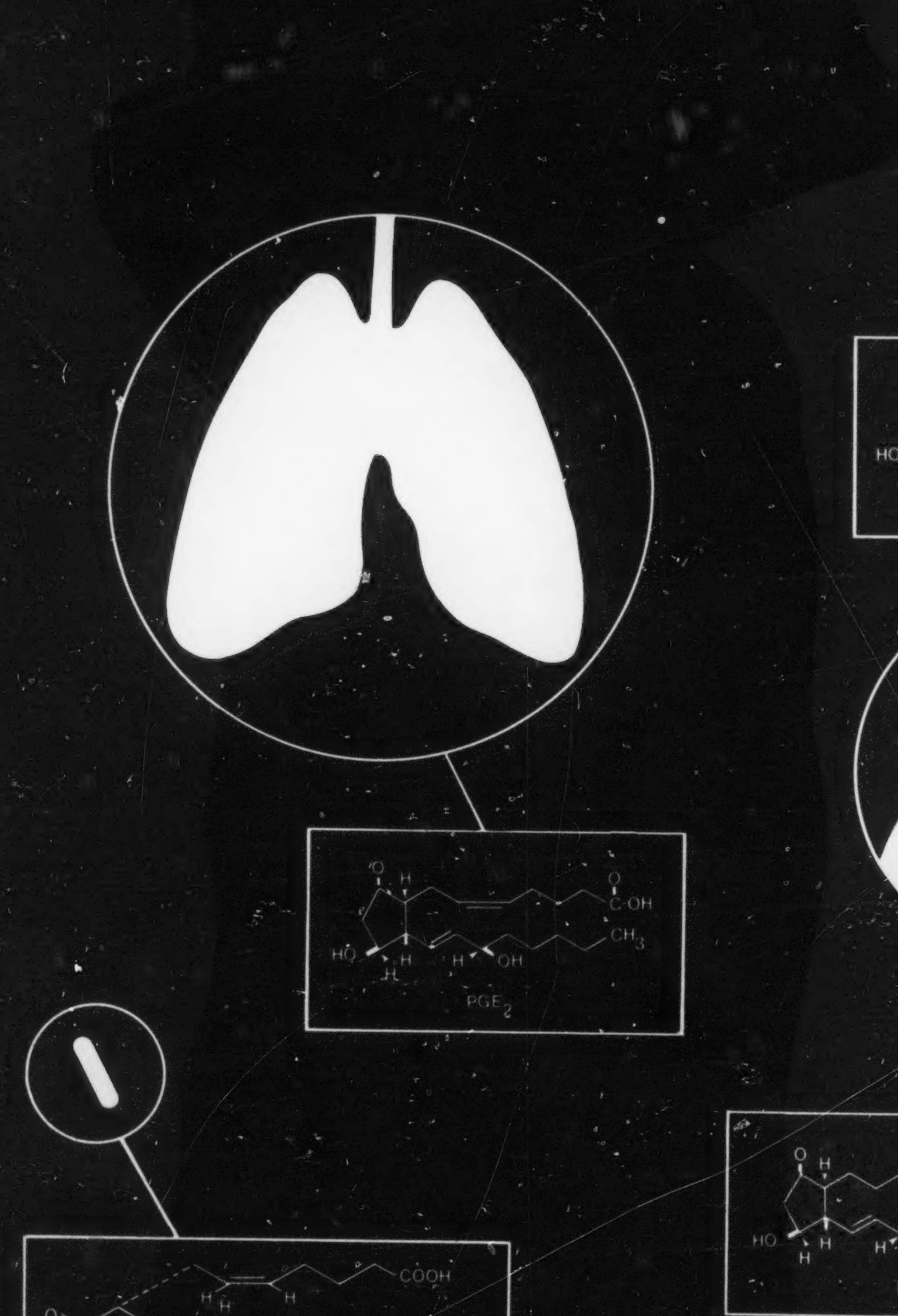
Buttkus also pointed to various studies which, he wrote, show that the difference in weight loss between waxed and unwaxed apples stored at 32 degrees Fahrenheit (0 degrees Celsius) is only 3.0 to 3.5 percent. He said still other data indicate that apples packed in polyethylene liners or bags and stored under the same cold storage conditions have a weight loss of only 0.5 percent. He also cited other studies that indicate the shelf life of waxed apples is lengthened by only one to three days.

A one-year study conducted for the Washington Apple Commission, a quasi-public body in that state, by the Institute of Biological Chemistry at Washington State University in Pullman included, in part, tests on whether the waxing of apples retarded water loss from the fruits during storage. This involved a comparison of both untreated apples with others to which one of five commercial wax formulations was applied. The weight loss of the treated and untreated apples (red delicious variety) over a six-month period in cold storage was then measured.

The study showed a weight loss of 3.12 to 4.69 percent for the untreated apples compared to a range of 2.23 to 3.21 percent for the waxed apples. It is quite clear, the report noted, that the waxing resulted in a measurable decrease in water loss during storage, demonstrating one of the beneficial effects of this post-harvest treatment. The same study also involved testing of whether any of the major wax formulations used in the state of Washington introduced any significant new wax components to the apples. The report concluded that the waxing process used does not introduce measurable amounts of foreign wax (new wax components) to the apple.

Chris Lecos is a member of FDA's public affairs staff.

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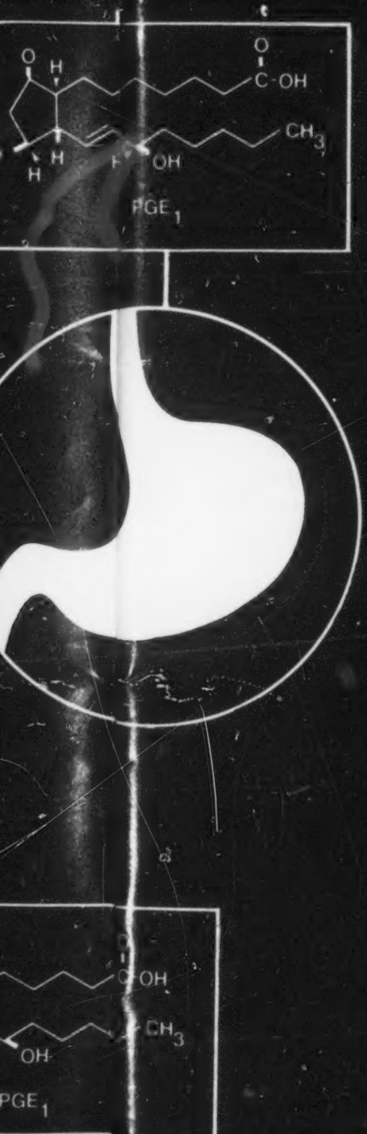
Prostaglandins Are Regulators Extraordinar



by Annabel Hecht

Never mind what the name sounds like—everyone has prostaglandins.

Prostaglandins are a family of compounds found in just about all human and animal tissues. These compounds are not stored in the tissues but are synthesized, or manufactured, out of essential fatty acids in a complex series of steps involving various enzymes.

Prostaglandins appear to be involved in the regulation of the way tissues respond to normal physiological stimuli and to injury. They probably are important in all tissues, although that has not yet been established.

Only small amounts of these substances are produced and in most cases they are quickly metabolized or processed and eliminated from the body. Yet they have wide-ranging and sometimes widely differing effects on practically all the body's biological functions. It may be that these differing effects create a balance that is essential to the prostaglandin regulatory role.

Among other things, prostaglandins affect blood pressure, sensitize the body to pain and fever, and are essential to the process of blood clotting. Although the therapeutic uses of prostaglandins are limited at this time, scientists have learned that drugs that inhibit, or slow down, production of prostaglandins help alleviate the pain of arthritis and other inflammatory conditions.

Research on prostaglandins got its start more than 50 years ago when two American gynecologists made the remarkable discovery that application of fresh human semen caused relaxation of strips of uterine tissue taken from women who had borne children while

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Prostaglandin-Inhibiting Drugs

Brand/Generic name	Indication
Anaprox naproxen sodium	Relief of mild to moderate pain Primary dysmenorrhea (menstrual cramps) Signs and symptoms of rheumatoid arthritis and osteoarthritis
Clinoril sulindac	Osteoarthritis Rheumatoid arthritis Ankylosing spondylitis (severe form of arthritis) Acute painful shoulder Acute gouty arthritis
Indocin indomethacin	Osteoarthritis Rheumatoid arthritis Ankylosing spondylitis Acute painful shoulder Acute gouty arthritis (where patient is unresponsive to salicylates)
Meclomen meclofenamate sodium	Relief of signs and symptoms of rheumatoid arthritis and osteoarthritis, but not as primary drug of treatment
Motrin ibuprofen	Signs and symptoms of rheumatoid arthritis and osteoarthritis Mild and moderate pain Primary dysmenorrhea
Nalfon fenoprofen calcium	Relief of signs and symptoms of rheumatoid arthritis and osteoarthritis Relief of mild to moderate pain
Naprosyn naproxen	Signs and symptoms of rheumatoid arthritis and osteoarthritis Mild to moderate pain and dysmenorrhea
Ponstel mefenamic acid	Relief of mild to moderate pain when therapy won't be longer than one week Dysmenorrhea
Tolectin tolmetin sodium	Signs and symptoms of rheumatoid arthritis and osteoarthritis (acute flares and long-term management) Juvenile rheumatoid arthritis
Zomax zomepirac sodium	Relief of mild to moderately severe pain

pounds has been called "awesome" and "bewildering" by some scientists. Now that synthetic versions of prostaglandins are available, research is being carried out on a global scale and much progress has been made in recent years in understanding the role of these compounds in human health and disease.

For example, scientists have learned that prostaglandins of the E and A series are potent vasodilators—that is, they relax the blood vessels and thus can lower the blood pressure. On the other hand another compound, $PGF_{2\alpha}$, constricts blood vessels and raises blood pressure. The E and G prostaglandins can also affect platelet clumping and thus blood clotting. PGE_1 increases the clumping of these tiny blood cells, while PGE_2 decreases this effect.

Different prostaglandins have different effects on the smooth muscles. For instance PGFs tighten the bronchial and tracheal (air passage) muscles, while PGEs relax those same muscles. In the gastrointestinal system, the E prostaglandins shorten the time it takes matter to pass through the intestines, but they cause diarrhea and cramps. At the same time prostaglandins appear to have a protective effect against injury to the lining of the gastrointestinal tract. That PGEs inhibit the secretion of gastric acid and pepsin suggests that some day they may have an important clinical role in the treatment of patients with ulcers.

Prostaglandins also appear to be a factor in keeping open the ductus arteriosus, a channel between the pulmonary artery and the aorta that exists in the fetus until shortly after birth. Usually the channel closes naturally when the baby begins to breathe on its own. If the channel doesn't close, heart failure may develop and surgery may be required. Doctors have found that the channel can be closed by administration of drugs that inhibit production of prostaglandins. The same drugs are used for treatment of arthritis and other inflammatory conditions.

Sometimes, if an infant has a certain type of congenital heart defect, it is important to keep the ductus open until corrective surgery can be performed. FDA recently approved a prostaglandin, alprostadil, for just such situations. Called an "orphan drug" by its manufacturer because of its limited use potential, the new drug is the first prostaglandin product approved for cardiovascular use. (See "Rx for Orphan Drugs," *FDA Consumer*, September 1980.)

In other research areas, scientists have found that prostaglandins apparently interfere with the way some pancreatic cells in diabetes patients "recognize" glucose, thus preventing the glucose from stimulating the release of insulin. Other research has suggested that prostaglandins have some part in the control of immunologic response by, among other things, inhibiting the activity of the so-called "killer" white cells in the blood.

Many of these research findings may lead to drugs in the future, but first there are some hurdles. For one thing, since each type of prostaglandin has a variety of effects on the body, it is hard to zero in on just one therapeutic use. In addition, the unwanted effects on other tissues may outweigh the desired one on the target tissue. Another problem is the relatively short life span of prostaglandins.

One line of research that led to the development of prostaglandin-containing drugs concerns the effect of these compounds on the female reproductive system. The very earliest studies showed that prostaglandins could relax or contract uterine tissue. Later research revealed that this effect was influenced by a woman's menstrual cycle. Apparently there is a high sensitivity to PGE_1 at mid-cycle near ovulation and an even greater sensitivity to $PGF_{2\alpha}$ just before menstruation and during pregnancy.

Four prostaglandins have been identified in amniotic fluid during labor and during spontaneous abortion. The concentration of these compounds appears to increase as labor progresses. There also is evidence that prostaglandins play a role in premature labor. The first clinical use of prostaglandins, to induce labor, was reported in 1968.

Three prostaglandin drug products, approved by FDA, may be used to terminate pregnancy during the second trimester, i.e., the second three months. One, a vaginal suppository, also may be used to treat intrauterine fetal death or to remove a rarely occurring tumorous mass called a hydatidiform mole that sometimes results from a failed pregnancy. All three drugs are to be administered by medically trained personnel in a hospital, where patients can be carefully monitored. Strict adherence to recommended dosage is a must.

Because prostaglandins work in animals very much the way they work in humans, uses for these compounds have been found in veterinary medicine as well. FDA has approved three prostaglandins of the $F_{2\alpha}$ class used to induce estrus (the "heat" stage) in horses and to synchronize estrus in cattle. This allows farmers to time the breeding of their stock. The drug approved for cattle also may be used to induce abortion in animals being held in feed lots prior to slaughter.

While prostaglandins are capable of doing good, under certain conditions they can also produce undesirable effects. For instance, scientists have long known that prostaglandins play a role in the sensation of pain. They do not actually cause it, but they set the stage by sensitizing nerve endings that transmit pain signals to the brain.

In 1971 a group of British researchers solved the age-old mystery of why aspirin relieves pain when they discovered that this common drug inhibits the manufacture of prostaglandins by interfering with one of the key enzymes in the biochemical chain of events. When the chain is broken, prostaglandin production decreases and pain and inflammation are improved.

Out of this knowledge has grown a class of drugs known as non-steroidal anti-inflammatory drugs or, as they are sometimes called, prostaglandin inhibitors. Besides aspirin, there are 10 prescription drugs of this type now on the market (see table). Most were used initially for the relief of pain and symptoms of rheumatoid arthritis and osteoarthritis. Like aspirin, they ease pain and inflammation but do not cure the underlying disease. Three of these drugs, mefenamic acid (Ponstel), naproxen sodium (Anaprox) and zomepirac sodium (Zomax) were developed to be used for the relief of mild to moderate pain.

Recently researchers have found another use for the prostaglandin-inhibiting drugs—treatment of dysmenorrhea, the painful cramps experienced by untold numbers of women during their menstrual period. It is estimated that 48 to 52 percent of ovulating women experience this uncomfortable condition and for 10 percent of these the cramps are severe. For years, women have been told that these cramps are "all in the mind" or that having a baby would solve their monthly ills.

In 1940 the demonstration that suppression of ovulation prevents dysmenorrhea suggested that there was a physical rather than a mental reason for cramps. Unfortunately, the psychological theory held fast. But 17 years later, in 1957, British scientist V. R. Pikles, suggested that something in the uterus itself might be the cause of the painful contractions. Using tampon samples of menstrual fluid from women with dysmenorrhea, he was able to extract what he called the "menstrual stimulant." This was later identified as prostaglandins. It is now known that women who have severe cramps produce more prostaglandins than women who have normal periods, although exactly why this is so is still a mystery.

Researchers began to put two and two together. If prostaglandins did cause severe cramps, prostaglandin inhibitors should stop them. Clinical trials with several of these drugs proved them right. So far four of the inhibitors have been tested in women with dysmenorrhea and have been approved by FDA for the relief of this type of pain. They are naproxen sodium (Anaprox), naproxen (Naprosyn), ibuprofen (Motrin and Rufen), and mefenamic acid (Ponstel). Studies of other prostaglandin inhibitors are in progress.

One of the primary advantages of the prostaglandin inhibitors is that they are not addictive as the narcotic painkillers are. Unfortunately, they still have side effects, which may include gastrointestinal disorders, nausea, vomiting, diarrhea, abdominal pain, constipation, kidney disorders, dizziness, sleepiness and skin rash.

Aspirin is the granddaddy of all prostaglandin inhibitors, though it is not as potent as some of the newer drugs in the class. Because of the close similarities, the new inhibitors should not be given to patients who are sensitive to aspirin, and in some cases they should not be given along with one another because they may be competing for their effects. This could result in higher or lower levels of one or the other drug.

Annabel Hecht is a member of FDA's public affairs staff.

All You Knead To Know About BREAD

by Harold Hopkins

Most Americans ate some bread yesterday and the day before, and will eat some more today and tomorrow. Daily bread is not just a figurative expression. It's aptly called the staff of life, and anybody without it suffers a deprived economic condition. The stuff is tied to our very existence. Bread, or something like it, is the one food common to every civilization past and present except for a few hunting or fishing peoples in hostile climates who have to make do with reindeer milk, seal blubber or others of nature's less likely bounties.

Not so many years ago almost everybody could think back to mom with her hands deep in dough and a smudge of flour on her cheek; but today most moms buy the family's bread already baked, sliced and wrapped at the neighborhood supermarket, where stale is a four-letter word and the bread ingredients often polysyllabic. Within the typical loaf reposes a product as white and silky as a bride's trousseau, that easily passes the squeeze test, that shows no hint of molding and, even after lying on the shelf at the grocery for several days, looks as if it were just turned out of the pan.

What we today call convenience foods probably started a long, long time ago with bread, and it's still the most popular of them all. Baking takes time and trouble that most of us would as soon be without, and advances in culture or affluence down through the ages appear to have been accompanied by a turnover of breadmaking chores to specialists—commercial bakers, at times the government, even the priesthood.

There's good evidence that making or baking bread dates at least to 7000 B.C. Egypt had public granaries, filled by tithes of grain against the possibility of famine, and workmen were paid their wages in grain, breadloaves or beer. Beer contains essentially the same ingredients and undergoes the same yeast fermentation (and in some African countries is brewed in a thick, highly nutritious form that still substitutes for bread). There were public bakeries in Greece in the 5th century, B.C. Rome had a public bread dole, which its emperors manipulated to keep down civil unrest. According to the Roman satirist, Juvenal, the Roman populace of his time cared for nothing but "bread and circuses." Public dissatisfaction with the bread supply reportedly was one of the grievances that led to the French Revolution.

In its larger meaning bread or substitutes for it can include loaves, rolls, buns, cakes, pones, scones, cookies, biscuits, crackers, hardtack, piecrusts, stuffings, spoonbread, pancakes, johnnycakes, hoecakes, popovers, hushpuppies, tortillas and the like, as well as pastas and other mixtures such as macaroni, noodles, dumplings, spaghetti, gruel, mush, porridge, hominy, and dry breakfast cereals, even popped grains. Breads and similar starchy edibles are made from grass seeds such as wheat, rye, barley, oats, millet, corn and rice; from legumes such as soybeans; and from bananas, buckwheat, artichokes, roots, tubers, kelp, acorns and a number of other foods and mixtures of foods. Bread may be leavened or unleavened and may be cooked by baking, frying, boiling or steaming, and doubtless by other ways.

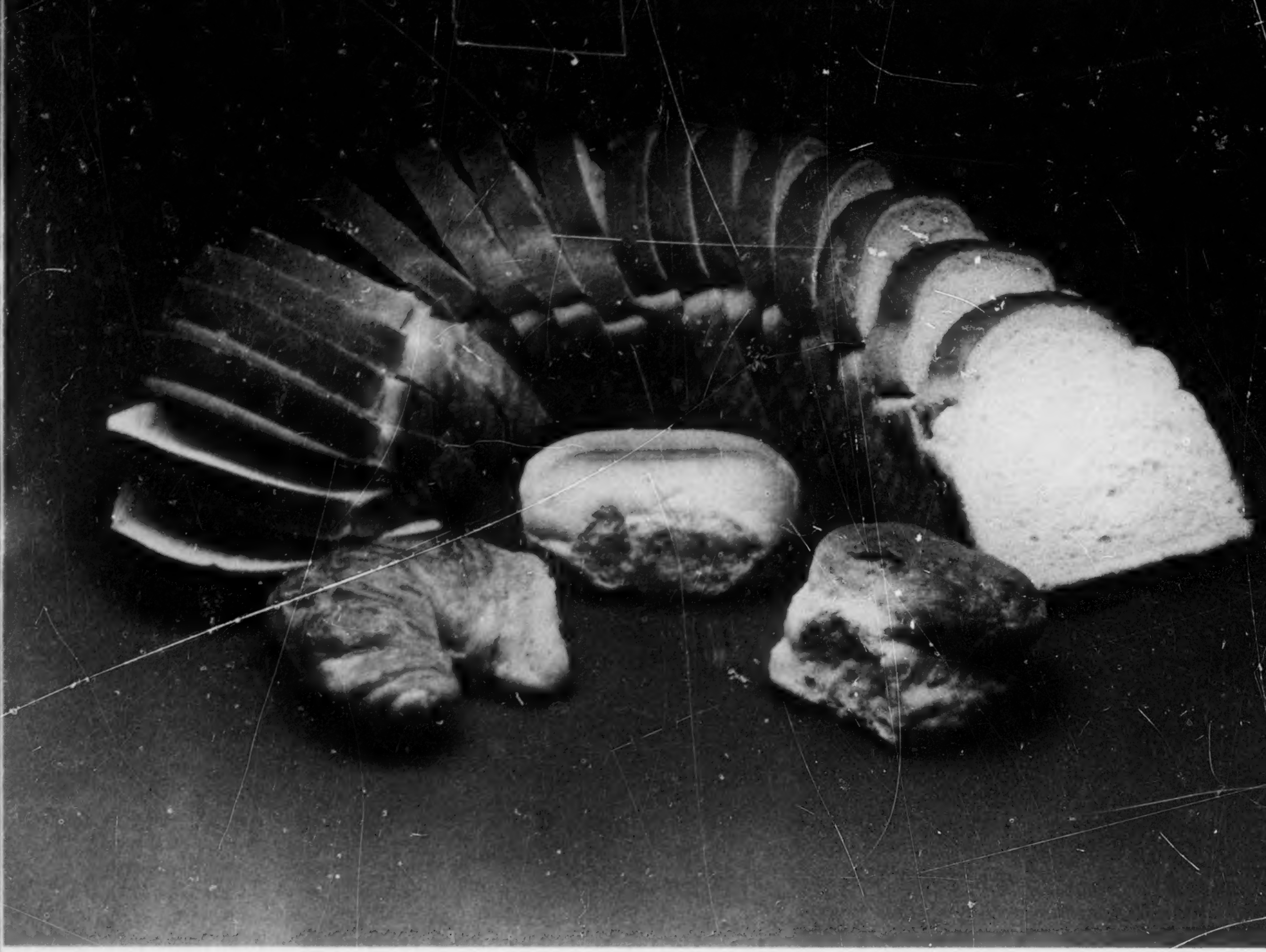
Ingredients often incorporated into breads for taste, flavor, or nutrition are salt, eggs, milk, honey, sugar, butter, raisins or other fruits, seeds such as poppy and sesame and nuts. Obviously, for a food so venerable, there has been a lot of experimentation and adaptation by both commercial and home bakers. The housewife may fight boredom or finicky palates by putting just about anything into the dough short of the kitchen sink. Onion, garlic, cheese, potato, and crackling bread, dateloaf, and sweet potato pone are pretty tame stuff to a baker who lets his fancy ramble a bit. The invention of the sandwich late in the 18th century, besides opening up new vistas in the kitchen and siring a whole subculture known today as "fast food," probably saved baking itself from utter absurdity.

It's still other ingredients, particularly those put into the store-bought sorts of bread, that give some of us pause these days; for the most part, however, there seems no real basis for concern other than an occasional uneasy feeling that so many of the unfoodlike names that make up the ingredient list are passing strange for a food we eat a very lot of every day of our lives.

To understand why so many of these substances seem to wind up in bread, we ought to look at some basics about the stuff—its physical properties, how it's made, the problems that arise when it's not eaten right after baking, and other difficulties related to its mass production, storage, transport and marketing.

The two main forms of bread are flat or unleavened cakes or wafers and raised or leavened loaves or buns. It's presumed that flat bread antedates raised bread by several centuries, but it all happened so long ago that nobody can say for sure. The speculation is that spores of wild yeast, a fungus, got into a mess of not-yet-baked bread dough by some accidental contamination and had such a salutary effect on the bread, and on those who tasted it, that the process bore repeating. Fortunately, once dough gets yeasty, a small piece can be saved to "contaminate" the next baking; that is, the new batch of dough can be given a yeasty start by a bit of the old. This is called sourdough baking, and that all-important piece of yeasty dough, called a starter, has at times in the past been a mainstay of civilization on the move, carried aboard the covered wagon, carefully nurtured in the forty-niner's backpack, and accompanying the lumberjack's and cowboy's dutch ovens. Alaskan gold rushers were known as Sourdoughs. Yeast's function was identified quite early, and granular and caked yeast were cultured for use in individual bakings, but sourdough baking remains a standby, and a treasured one, in places where

GRANDMA'S MOLASSES
Natural Yeast



the grocery store may be a hundred miles away.

In the last couple of centuries, chemical leavening agents have been developed, first baking soda and then baking powder, which combines baking soda with acids. These agents have been responsible for new departures in baking and new families of baked goods.

Leaveners do their job by expanding and making the dough springy or elastic, therefore more eatable. Yeast leavening takes place by fermentation in the dough at room temperature. Fermentation creates carbon dioxide gas as a by-product, and this expands and is captured in uniformly sized pockets in the dough mixture that hold the gas until the dough dries, giving it a soft texture. Fermentation is a life process of the fungi and thus takes some time.

Leavening by chemical agents also involves expansion of carbon dioxide, but this takes place mostly in the oven as heat completes the chemical reaction that makes the bread rise. "Double acting" baking powder, the most popular chemical leavener, expands the dough both during mixing and in the oven. Breads baked with chemical leaveners are known as quick breads because baking can be started immediately after the dough is mixed without waiting for fermentation to take place. Such chemical agents have had a profound effect on home baking habits. Many flour products sold for baking today include chemical leaveners (and other ingredients) that are already incorporated—self-rising flour, for instance. If th
were not enough for America in a hurry, we now have
ready mixed and rolled "instant" doughs that are froze
or refrigerated and ready to pop into the oven for baki
or browning.

Yeast-leavened and chemically leavened breads have
essentially two things in common: They use the same c
eal grains and they both are raised. But from there the
resemblance gets shakier. Yeast breads expand to larg
bulk, are more palatable, have a closer grain with thin
cell walls, and are of a more silky texture. Quick bread
do not expand so much, are denser, and have a coarse
grain and a crumbly texture. Yeast breads are mainly i
the form of loaves, rolls and buns, and can be stored
without refrigeration and eaten cold with almost as mu
satisfaction as when hot. Many quick breads, such as pa
cakes, biscuits, cornbread and waffles, do not taste nea
as good cold as they do hot, though a few quick bread
types such as gingerbread and cookies go well either w

A few products, angel cake and sponge cake, for instance, are leavened by rapid beating of ingredients su
as egg whites or repeated folding of the dough to captu
air in it. Some liquids are also used in a puffing proces
for making hollow pastries.

Without doubt, leavening agents are the ingredients most responsible for making bread the delightful eating it is, but the real magic of baking comes from something called gluten, already in the flour. Gluten occurs in several cereal grains, notably wheat, in some varieties constituting as much as 11 percent. Next in gluten content is rye, with substantially less. Some grains—corn, barley, millet and buckwheat—really don't contain enough gluten to make raised breads. Wheat flour, because of its high gluten content, especially the white or bleached variety, is often mixed with some flours wanting in gluten to improve their texture, edibility and rising capacity in baking. People in the northern parts of Europe once depended almost entirely on barley and rye for bread because they had no strain of wheat hardy enough to cultivate, but eventually hardier strains were found. At the end of the 18th century only 5 percent of the bread eaten in England was made from rye, compared to 40 percent a hundred years earlier. The lowly barley was considered fit only for the poor and for livestock, though it has remained important in brewing and distilling.

About 80 percent of wheat's protein content is gluten, which is insoluble in water. When water and flour are mixed to make dough, the mixture is held together by the gluten, whose chainlike molecules join to create a film that becomes an elastic or resilient network. This network entraps the carbon dioxide gas from the leavening process and forms more or less uniform pockets or cells. These enlarge to expand the dough as yeast fermentation begins, or reaction from chemical leavening occurs upon mixing and heating in the oven. Variations in gluten content govern the baking quality of flour, making the dough soft and expandable, tough and plastic, or in between. Gluten is not merely versatile; it's the key to proper baking of any raised bread product.

Wheat's protein content is far more nutritious than was once supposed. The protein and other nutrients in bread and flour make them nutritious staples in the diet. Bread's universal use and its potential for nutrition were major factors in a decision in 1941 by federal government health authorities and the flour and baking industries to select bread as the ideal "carrier" for certain essential nutrients to be added. This plan for "enrichment" of breads and flours by the addition of nutrients gave reasonable assurance that just about everybody would get increased amounts of the three added vitamins: thiamine, niacin and riboflavin. FDA's standards for breads, for flours, for wheat-based cereals and for macaroni and noodle products today provide an enriched category for each that also includes some iron and, optionally, calcium. This enrichment helps offset losses of nutrients from processing, mainly the bolting of flour from the grain by machinery. Today more than 95 percent of all commercial white bread is enriched. This program has contributed to a significant decline in certain diseases, such as pellegra, that had resulted from deficiencies of vitamins or minerals in some segments of the U.S. population before 1941.

Bread, because of its importance to the nutrition and economy of the entire population, has always commanded priority in food law and regulation. The assumption of grain storage, milling and baking functions by commercial interests carries with it an implicit opportunity for adulteration, short weighting and other economic deceptions, and can also potentially affect public food safety because of the large numbers of people who eat the products of one processor. In this country commercial bakeries produce more than 95 percent of the bread consumed.

FDA watches bread in the making, labeling, shipping and storing. Agency inspectors visit commercial grain storage places, food warehouses, transports and the waterfront, and also go where bread is being mixed and baked. FDA personnel check for filth, bacterial contamination, pesticide residues and traces of other chemicals or substances that don't belong in bread, or any food.

The baking industry looks at bread closely, too. It has to. The biggest problem with bread, ordinary bread, is that it starts to stale the moment it comes out of the oven. When bread stales, the starch crystallizes and the bread hardens. Mold also sets in if bread is not used in a reasonably short time. Mass producing bread and marketing, transporting and storing it can introduce a slew of problems.

Today, staling is less of a problem to bakers because they use "bread emulsifiers," which keep the bread from going hard. Some of these, such as the synthetic emulsifiers called monoglycerides and diglycerides, are also used in cakes, doughnuts and other baked goods to produce desirable volume and textures. Polysorbates also are used to improve the texture of cake mixes. Lecithin from soybeans is a natural emulsifier used in cake mixes.

In times past, the growth of mold on bread and other baked goods was a major problem for bakers and their customers. Today bakers use calcium propionate or sodium propionate, and in some breads and cakes sodium diacetate is used to retard mold.

Dough conditioners such as calcium stearyl-2-lactylate and sodium stearyl fumarate are added to make bread dough drier, stretchier and easier to handle with machines, often in combination with the glycerides. In the "good old days," bakers had to store or set aside their flour in bins for months after it was ground to let it "age" or "mature." Otherwise the dough ended up as a sticky mass that wouldn't rise well and made poor quality bread or rolls. Then a few decades ago millers learned how to "age" or oxidize the proteins in the flour with chemicals, some of which also bleach the flour white. Maturing agents make it possible to use flour immediately, saving space and time and mitigating the risk of having the flour become spoiled or contaminated or eaten by vermin. Some maturing or bleaching agents are acetone peroxide, chlorine dioxide and potassium bromate or iodate.

The mouthful of additives you read on the ingredient list of a loaf of bread all have been approved by FDA under the food additive amendments. They're safe to use in stipulated quantities to perform the functions mentioned above, and others. They perform these very well and in doing so help make it possible for the busy householder to do other things than baking. There is plenty of precedent for modern housewives to bypass this chore, although it's not likely that their Greek or Egyptian counterparts of long ago were ever invited to go through the marketplace giving bakery products a quick squeeze here and there.

Harold Hopkins is editorial director of FDA Consumer.

X-rays For Childbirth: Risky, Costly, Not Always Helpful

by Roxanne Smith

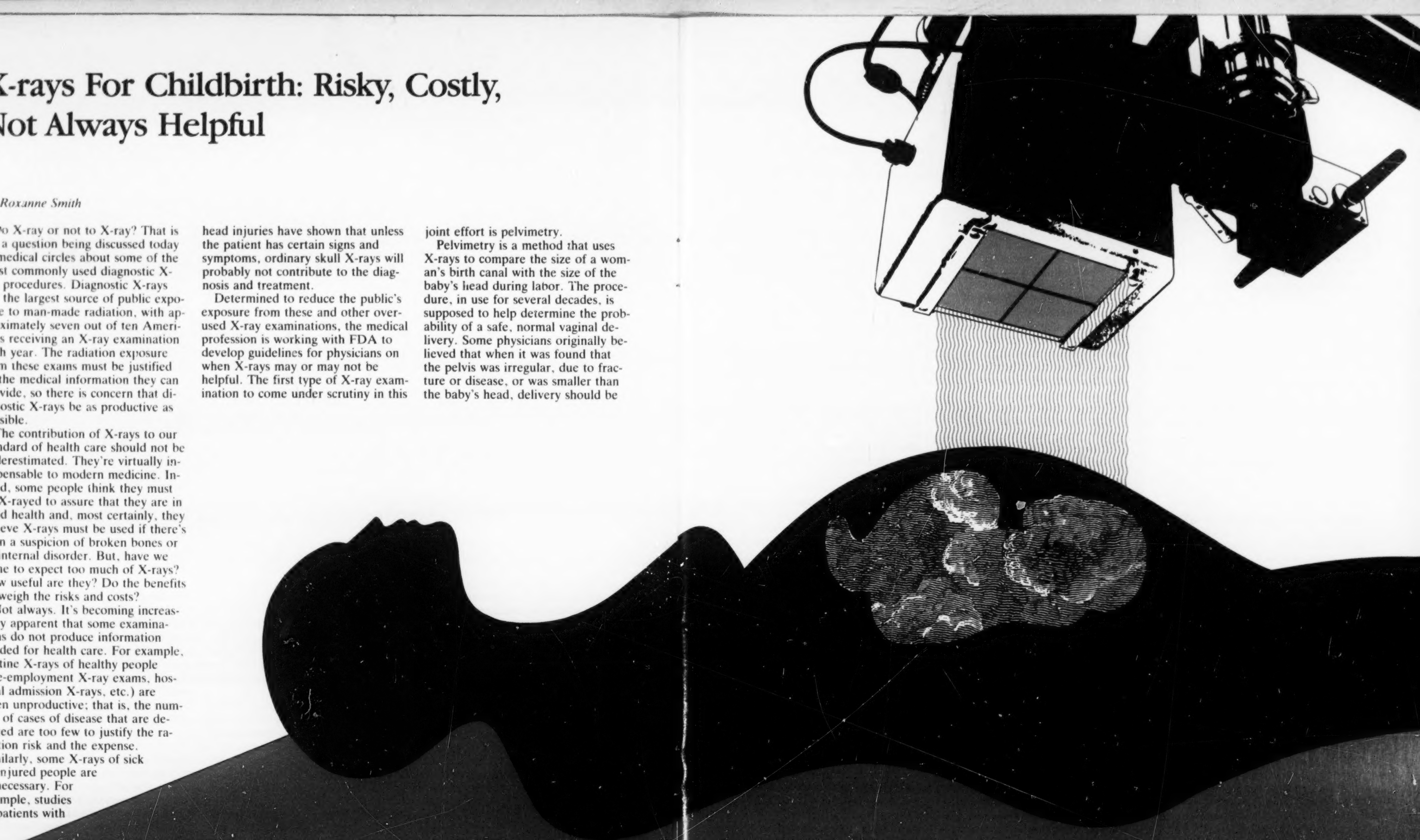
To X-ray or not to X-ray? That is a question being discussed today in medical circles about some of the most commonly used diagnostic X-ray procedures. Diagnostic X-rays are the largest source of public exposure to man-made radiation, with approximately seven out of ten Americans receiving an X-ray examination each year. The radiation exposure from these exams must be justified by the medical information they can provide, so there is concern that diagnostic X-rays be as productive as possible.

The contribution of X-rays to our standard of health care should not be underestimated. They're virtually indispensable to modern medicine. Indeed, some people think they must be X-rayed to assure that they are in good health and, most certainly, they believe X-rays must be used if there's even a suspicion of broken bones or an internal disorder. But, have we come to expect too much of X-rays? How useful are they? Do the benefits outweigh the risks and costs?

Not always. It's becoming increasingly apparent that some examinations do not produce information needed for health care. For example, routine X-rays of healthy people (pre-employment X-ray exams, hospital admission X-rays, etc.) are often unproductive; that is, the number of cases of disease that are detected are too few to justify the radiation risk and the expense. Similarly, some X-rays of sick or injured people are unnecessary. For example, studies of patients with head injuries have shown that unless the patient has certain signs and symptoms, ordinary skull X-rays will probably not contribute to the diagnosis and treatment.

Determined to reduce the public's exposure from these and other overused X-ray examinations, the medical profession is working with FDA to develop guidelines for physicians on when X-rays may or may not be helpful. The first type of X-ray examination to come under scrutiny in this joint effort is pelvimetry.

Pelvimetry is a method that uses X-rays to compare the size of a woman's birth canal with the size of the baby's head during labor. The procedure, in use for several decades, is supposed to help determine the probability of a safe, normal vaginal delivery. Some physicians originally believed that when it was found that the pelvis was irregular, due to fracture or disease, or was smaller than the baby's head, delivery should be



made by Caesarean section. But over the years pelvimetry also came to be used when the physician was considering a Caesarean delivery for reasons other than a small pelvis; for example, in the case of multiple births (twins or triplets) or with a breech (feet first) presentation.

As early as the mid-1930s, clinical researchers began to question the usefulness of pelvimetry. These doubts increased with the growing awareness of other factors. First, the small, trouble-causing pelvis is less common than in the days when bone-deforming diseases, such as rickets, were more prevalent. Second, strong uterine contractions in most cases cause the baby's head to "give" sufficiently for a safe vaginal delivery; the amount of this "giving" cannot be accurately predicted from the pelvimetry examination.

Thus, whether a woman is going to need a Caesarean section because of a "borderline" pelvis size or weak uterine contractions usually cannot be determined by pelvimetry. Finally, with the variety of diagnostic imaging tools available today (such as ultrasound, which does not subject mother or child to X-ray exposure), the need for Caesarean section can often be determined without pelvimetry. The consensus within the medical community presently is that the decision to use pelvimetry should be made on a case by case basis.

Experts have been concerned about pelvimetry not only because of its questionable usefulness, but because it is the single largest contributor of X-ray exposure to unborn children in the United States. Scientists suspect that irradiation during pregnancy can increase a newborn's chances of developing cancer later in life. Moreover, because the reproductive organs of mother and child are exposed during the examination, both are at greater risk of genetic damage, which can be passed on to future offspring. On a statistical basis, the increased risk of cancer or genetic effects from a pelvimetry procedure is very small for any given individual. So the benefit of a pelvimetry examination that is *needed* for the well-being of mother and child far outweighs the risk. On the other hand, unneeded pelvimetries expose mother and child to an unnecessary risk, however small.

Although the limited usefulness of pelvimetry has been generally known for some time, recent studies have shown that pelvimetries are performed in about 6 percent of all deliveries in the United States. (Total births in the United States in 1979 were 3,394,398.) The 6 percent rate was similar to that found 20 years ago. The studies also show that use of pelvimetry varies considerably from one hospital to another, with some using it in up to 50 percent of deliveries. Further, although pelvimetry is intended for use during labor, a study of one group of hospitals showed that 20 percent of all pelvimetries were being performed on an outpatient basis, well before labor, and well before any measurement could be of clinical value.

Besides the radiation risks to mother and child, there are substantial dollar costs to the public from the use of pelvimetry. At an average cost per exam of $50, pelvimetry is costing Americans $10 million a year.

Because of the growing body of information about the lack of pelvimetry's usefulness, a panel of leading obstetricians and radiologists met in 1979 under the sponsorship of FDA's Bureau of Radiological Health to review the scientific studies and clinical evidence on pelvimetry and develop appropriate guidelines for its use. The panel made this recommendation against routine use: "Pelvimetry is not usually necessary or helpful in making the decision to perform a Caesarean section. Therefore, pelvimetry should be performed only when the physician caring for the patient feels that pelvimetry will contribute to the decisions concerning diagnosis or treatment. In those few instances, the reason for requiring the pelvimetry should be written on the patient's chart. This statement does not apply to X-ray examinations for purposes other than measurement of the pelvis."

The statement was reviewed by the American College of Radiology and the American College of Obstetricians and Gynecologists (ACOG). The radiologists' group approved and adopted the statement. ACOG adopted a similar statement as policy: "X-ray pelvimetry provides limited additional information to physicians involved in the management of labor and delivery. It should not be a prerequisite to clinical decisions concerning obstetrical management. Reasons for requesting X-ray pelvimetry should be individually established."

More recently, FDA and the Health Care Financing Administration sponsored a program in 191 hospitals to make physicians more aware of the panel statements and the limited usefulness of pelvimetry. Preliminary information indicates that there has been a reduction of more than 50 percent in the use of pelvimetry in these hospitals, as a result of the education program.

The mother-to-be can also help in reducing X-ray exposure to herself and to her unborn child. She should feel free to ask questions and to discuss possible treatments and procedures, including pelvimetry, during prenatal office visits. If her doctor says that pelvimetry may be needed, she will want to understand why, and whether another procedure could provide the needed information. She should remember that the question is not so much risk as *usefulness*, that the benefit of a *needed* pelvimetry far outweighs the very small risk.

To X-ray or not to X-ray? The answer is "yes" in certain cases where pelvimetry is medically needed. But, for the vast majority of pregnant women, experts on pelvimetry from the medical community and from government agree, the answer is "no."

For more information on pelvimetry, copies of the FDA publication *The Selection of Patients for X-Ray Examinations: The Pelvimetry Examination* (Stock #017-015-0017401) are available for $2 each. Send a check or money order to Superintendent of Documents, Government Printing Office, Washington, D.C. 20402.

Roxanne Smith is a health educator in FDA's Bureau of Radiological Health.

The Tanning Pill, A Questionable Inside Dye Job

by Louise Fenner

You take a pill. You get a tan. Welcome to the 1980s.

It is a new twist, tanning from the inside out. No more drying sun, scorching tanning booths, or lotions that leave the user with streaks and blotches. These pills contain two food colors, chemical replicas of substances that occur naturally in some plants. After a week or two the dye accumulates in the skin, and voila! A tan!

But there's a catch. For one thing, the tan doesn't look quite right. It has a distinct orange tinge, especially on the palms and soles of the feet. And the unwary will soon enough find that the "tan" is no protection against sunburn. It's merely a dye job, and a costly one at that. The pills range from about $20 to $30 for a month's worth.

But more important, tanning pills have not been tested for safety. Although they contain the same color additives that go into many processed foods, the quantity of color additive in a day's supply of tanning tablets may be 20 or 30 times what would be consumed in a normal diet. Only one ingredient—beta carotene—has been studied extensively enough to warrant any judgment about its safety in large doses.

First developed in Europe, tanning tablets quickly surfaced in Canada and, about a year ago, in the United States. They contain synthetic versions of the natural coloring substances beta carotene and canthaxanthin (pronounced cán-tha-zán-thin), which belong to a family of compounds called carotenoids. These are responsible for much of the yellow, orange and red coloration in plants.

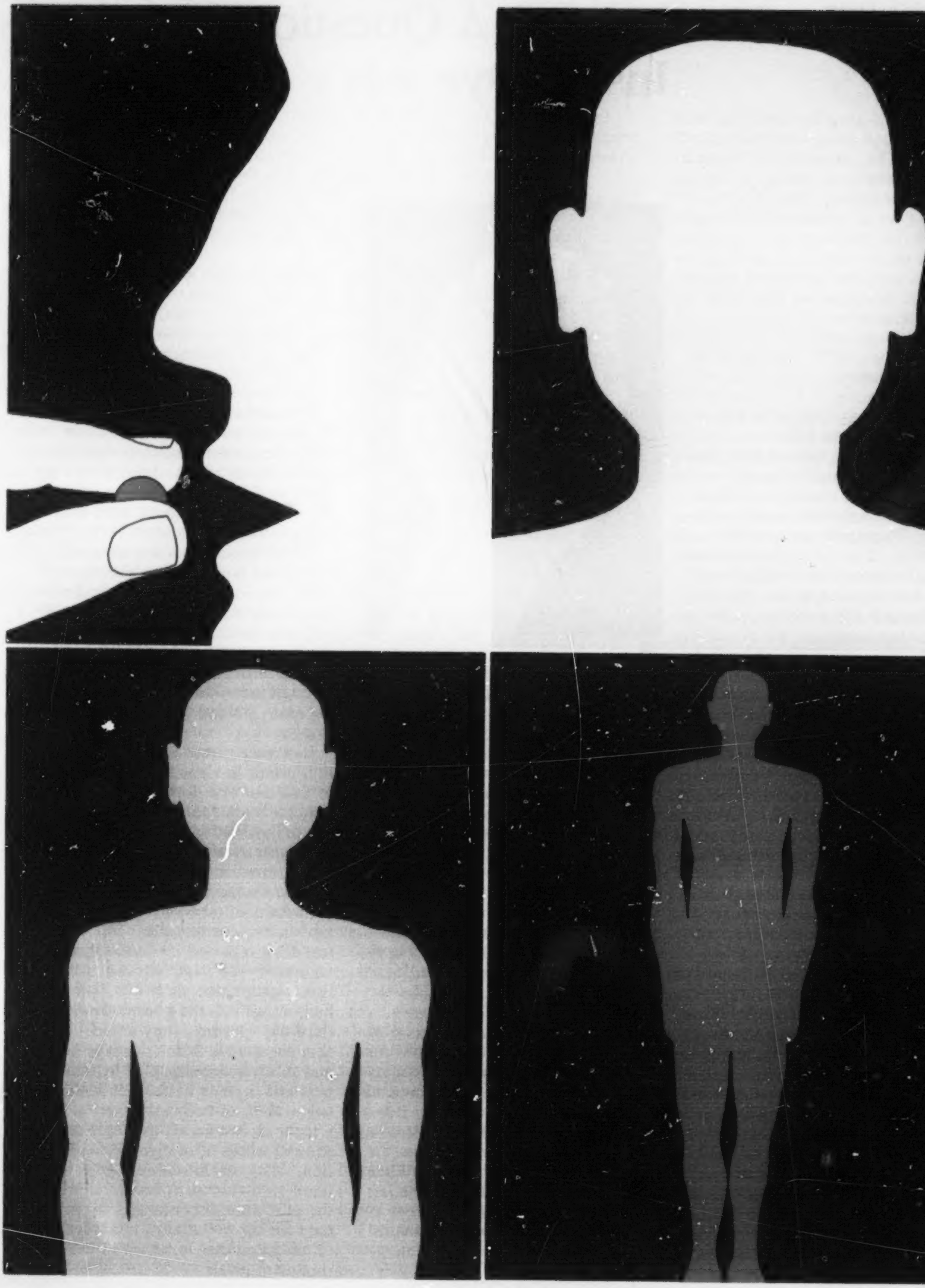
Beta carotene gives carrots, apricots, peaches, melons and other yellow fruits and vegetables their distinctive color. It is also found in green leafy vegetables, although the yellow color is masked by the green of chlorophyll. Canthaxanthin is a deep red-orange and is usually the predominant color in tanning tablets—sometimes the only one. Canthaxanthin appears in some plants, mushrooms, bacteria, brine shrimp, crayfish, sea trout, some algae and other forms of marine life, and in the water birds that feed on them. It is what makes a flamingo look like a flamingo.

The effects of tanning tablets start showing up as an "outdoor glow" to the person's skin about a week after the first swallow. Labels recommend taking several tablets a day for two or three weeks, then smaller doses to maintain the color. Dosages are based in part on body weight. When the palms get orange-tinged, the labels say it's time for the tanner to cut down. If the pills are discontinued, the color fades at about the same rate as it appeared.

Some labels caution pregnant women to consult a doctor before trying the tablets, which is excellent advice. Even better advice: Don't try them at all during pregnancy since the effect they may have on a developing fetus is unknown.

What tanning pills do, essentially, is give the body such an overdose of color that some of it accumulates in the blood, skin, fatty tissue and certain organs such as the liver. The dose is enough to tint the skin even though most of the color passes through the system unabsorbed, giving many potential tanners brick-red stools.

Last year nurses at a blood collection center in Canada were startled to find that one donor's plasma (the liquid left after the blood's red cells are sedimented out) was a bright orange instead of the usual pale yellow. The donor had been taking tanning tablets. Canadian doctors then asked volunteers to take various tanning tablets for several weeks. The doctors later reported in *Lancet* that one volunteer who took four canthaxanthin-based tablets daily for 37 days had orange-colored plasma from the third day onward. They noted, "The skin acquired a definite orange hue and this was accompanied by itchiness and dryness of the skin with discolouration of body secretions so that a tissue drawn across the forehead showed traces of orange pigmentation." The canthaxanthin also interfered with vitamin A analyses. When the pills were discontinued, it took 10 days for the volunteer's blood levels of canthaxanthin to return to pretreatment levels.



It has long been known that eating large amounts of carrots or other foods containing beta carotene can turn the skin yellow. The medical term for that condition is carotenemia. Although most people don't consider it attractive, carotenemia is not believed to be harmful. The color disappears when the source of beta carotene in the diet is reduced.

Carotenemia is the chief side effect of a prescription medication containing beta carotene that helps prevent photosensitivity in people with an inherited skin disorder called EPP (erythropoietic protoporphyria). Victims of EPP develop burning and itchy skin and sometimes skin lesions and ulcerations when they are exposed to the visible radiation of the sun. Beta carotene safely provides a defense against photosensitivity, but it does not protect EPP victims from sunburn, which is caused by the sun's invisible ultraviolet radiation. Similarly, the high doses of beta carotene and canthaxanthin in tanning pills offer no sunburn protection to normal users.

Beta carotene performs an important function in the body, since part of the carotene consumed each day is converted to vitamin A. Fortunately, the body regulates this process and limits the conversion of excessive levels of beta carotene. Thus, the beta carotene in tanning pills does not appear to pose a threat of vitamin A overdose. Canthaxanthin is not converted to vitamin A in humans and, in fact, some question exists as to whether it could interfere with the conversion of carotene to vitamin A. Studies indicate that it may offer some protection from photosensitivity for EPP victims, but canthaxanthin has no other known function in the human body.

Both carotene and canthaxanthin are approved by FDA as color additives in foods and drugs, and beta carotene is also approved for use in cosmetics. They are generally produced synthetically instead of being extracted from natural sources. The colors are used to enhance the appearance of foods such as pizza, barbecue and spaghetti sauce, soups, salad dressing, fruit drinks, baked goods, pudding, cheese, catsup and margarine.

The amounts of color put into such foods are a fraction of what is found in tanning tablets. A 1979 study of beta carotene as a food ingredient estimated that in a normal diet a person's intake of beta carotene added during processing would be about .3 milligrams (mg) daily. For canthaxanthin the estimate is 5.6 mg daily, based on calculations done by the manufacturer in a 1969 color additive petition (request for marketing approval). In comparison, one popular brand of tanning tablet contains 4 mg beta carotene and 36 mg canthaxanthin. With a recommended start-up dose of three or four tablets per day, the resulting intake would be 12–16 mg beta carotene and 108–144 mg canthaxanthin.

Neither substance is approved for use in ingested products intended to color the human body. According to the Food, Drug, and Cosmetic Act, manufacturers must petition FDA for approval of any new use of a color additive. FDA's decision on such petitions is made on evidence provided by the manufacturer—based in large part on animal studies—that the color is safe for the proposed new use. Therefore, until FDA gives its approval, the use of beta carotene and canthaxanthin in oral tanning products is illegal.

FDA is investigating tanning tablets and has taken some regulatory actions to keep them off the market. The agency has refused entry to some 40 shipments of tablets manufactured outside the United States and is maintaining an import detention alert on further shipments. One petition for the use of canthaxanthin in an oral tanning preparation has been submitted to FDA and is currently under review.

In 1981, FDA received two complaints from consumers who suffered adverse reactions after trying tanning tablets. A young woman in South Carolina experienced severe nausea, diarrhea and stomach cramps after taking the tablets daily for two months. Her doctor diagnosed her symptoms as "drug-induced" hepatitis, which he felt was caused by the tablets. She was hospitalized for five days, improved rapidly with treatment, and has reported no recurrences since discontinuing the tablets. A 23-year-old North Carolina man who took eight tanning tablets over a two-day period suffered severe itching and welts that covered his entire body. His symptoms lasted several days and were finally relieved by prescribed medication.

It is a good bet that neither of these consumers will be tempted to try a bottled tan again. "Anyone who saw or heard about me was too scared to take tanning tablets themselves," the North Carolina man commented. His reason for experimenting with the tablets offers a lesson in why they have become popular: "I wanted a suntan like everyone else, and I was too lazy to spend hours lying out in the sun, so I was trying to take the easy way out."

Whether the tanning tablets were the direct cause of these two reactions, or were taken coincidentally, is uncertain. However, the incidents demonstrate the need for additional testing of the color additives in the tablets.

Much more is known about beta carotene than canthaxanthin because of its prevalence in the diet, extensive nutritional research, and because animal and human safety studies were done in the early 1970s to support beta carotene's use as a drug in treating photosensitivity. Micheline Mathews-Roth, M.D., principal research associate at the Harvard Medical School and a former researcher on the beta carotene drug studies, found that about a third of the patients in the studies developed temporary nausea, cramps and diarrhea. Yellow skin color was the only other significant side effect.

Although much is known about carotenoids in general, canthaxanthin is one member of the family that has been somewhat neglected. One of Mathews-Roth's concerns is that the quantity of canthaxanthin [illegible] the tanning pills approaches the levels of beta carotene approved for use as a drug. "These doses (of canthaxanthin) are in the range used for the treatment of photosensitivity in EPP (30 to 300 mg beta carotene)," she said. "It is imperative that canthaxanthin receive the same in-depth toxicity testing that it would need if it were being marketed as a drug for the treatment of photosensitivity."

Mathews-Roth summarized her views: "I would warn people not to take tanning pills until appropriate well-controlled studies are done on canthaxanthin, until we are sure there is no long-term toxicity."

Louise Fenner is a member of FDA's public affairs staff.

The Notebook

The Notebook: a potpourri of items of interest to consumers, gathered from FDA press releases, other news sources, and *Federal Register* notices. The *Register* items are designated FR for reader convenience. The *Federal Register* is usually available in large public libraries.

■ The sodium and potassium content of everyday foods plus some suggestions on how to flavor your food without salt are featured in a brochure "**Sodium Sense**," developed by the Food Marketing Institute in cooperation with FDA and the National High Blood Pressure Education Program. A limited number of single copies are available from FDA's Consumer Communications, 5600 Fishers Lane, Rockville, Md. 20857, and from the Food Marketing Institute, 1750 K St., N.W., Washington, D.C. 20006 (include a self-addressed, stamped envelope). Multiple copies can be purchased from the institute, which will provide price information on request.

■ A proposed rule that would have required medical device manufacturers and distributors to submit **reports on deaths**, injuries and other problems to FDA is being held in abeyance until further notice. Most public comments on the proposed rule opposed it. At the same time, FDA withdrew a proposed rule that would have restricted the sale, distribution and use of certain types of medical devices to health professionals (FR Nov. 24).

■ **Allergenic extracts** labeled "No U.S. Standard of Potency" are now exempt from FDA requirements for expiration dating and stability testing. Because there is no standard by which to measure potency, such tests cannot be conducted (FR Nov. 17).

■ Effective Dec. 24, 1981, blood donors at **plasmapheresis centers** who are to be immunized for the production of high-titer plasma will not need to be re-examined before the first immunization injection if they have already had a physical examination for plasmapheresis. This rule eliminates a burden on donors and centers (FR Nov. 24).

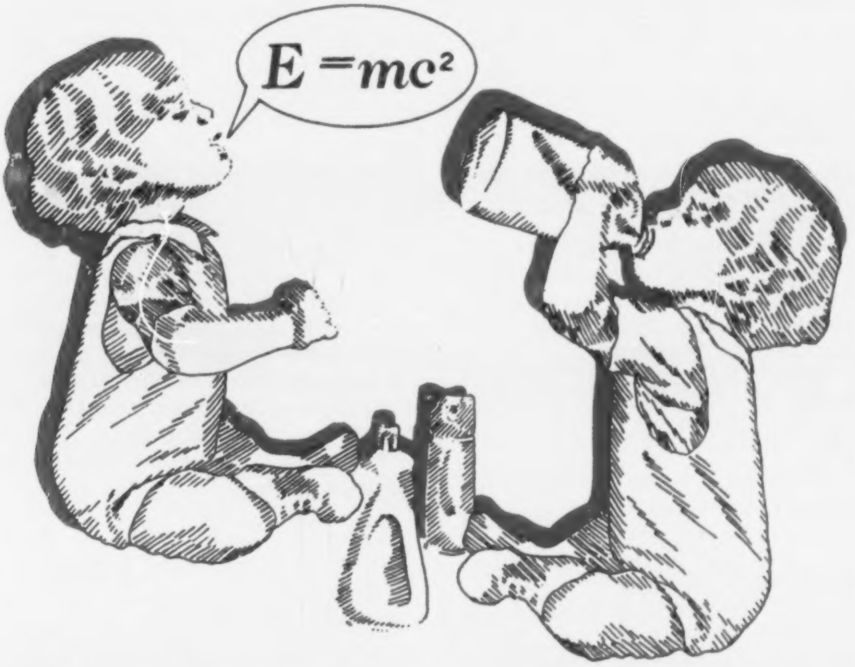
■ DMSO, the controversial and unapproved **arthritis remedy**, has been found to alter the metabolism of sulindac, a prescription drug widely used to treat the disease. Brian N. Swanson, Ph.D, of Thomas Jefferson University Hospital, Philadelphia, said data from studies with laboratory rats suggest that using the two drugs together might initially diminish sulindac's therapeutic effect, but might actually enhance it later.

■ FROM THE MARKET BASKET: FDA has executed a memorandum of agreement with Mexico's Secretariat of Health and Welfare to assure that fresh and **fresh-frozen oysters**, clams and mussels exported to the United States are safe, wholesome and conform to the standards of both countries (FR Dec. 1). . . . FDA has published the Recommended International **Standard for Raisins** developed by the Codex Alimentarius Commission. The commission, jointly sponsored by the Food and Agriculture Organization and World Health Organization, develops worldwide food standards. Food that complies with the Codex standard may move freely in U.S. interstate commerce. FDA cannot establish its own standards for dried fruit (FR Nov. 13). . . . U.S. standards of identity for **canned pineapple** have been amended to redesignate as "small cubes" or "dice" the style now referred to as "cube" or "dice" and to provide for an additional optional style, "large cubes." The rule becomes effective July 1, 1983 (FR Nov. 24). . . . Effective the same date, ascorbic acid, erythorbic acid and their sodium salts may be used to **preserve color** in "white" and "green-tipped and white" asparagus (FR Nov. 17). . . . In the proposal stage are standards of identity for **goat's milk ice cream**, goat's milk frozen custard, and goat's milk ice milk to be cross-referenced to the standards of identity for ice cream, frozen custard and milk (FR Dec. 8).

■ FROM OTHER REGULATORY AGENCIES: The rule that would have required ingredient **labeling on wine**, distilled spirits and malt beverages has been rescinded by the Bureau of Alcohol, Tobacco and Firearms (FR Nov. 6). . . . Drug Enforcement Administration puts **alprazolam** in Schedule IV of the Controlled Substances Act (FR Nov. 12) and withdraws proposed Schedule I designation for tiletamine and zolazepam. Preparations containing equal amounts of these substances remain in Schedule III (FR Dec. 8).

Investigators' Reports

Into The Mouths Of Babes . . .



Out of the mouths of babes may come wisdom, but into the mouths of babes go too many unwise things. In fact, into those young mouths go a startling array of substances adults would not dream of eating unless they were trying to harm themselves.

FDA's National Clearinghouse for Poison Control Centers continually receives reports of children under age 5 swallowing such repellent substances as turpentine, gasoline, moth balls, rat poison, bleaches, oven cleaner, antifreeze and insecticides. Older children also may become victims of poisoning, but they are likely to have a reason for swallowing a drug or other substance. In children under 5, curiosity is reason enough.

When reports from poison control centers were tallied by FDA for year 1979 (the most recent published data available), nearly 60 percent of the 144,262 incidents involved children under five. Most of the youngsters were unharmed, but at least seven died (three other death reports did not include age), and nearly 10,000 suffered illness. These numbers are only the tip of the iceberg.

The information comes from approximately 325 poison control centers around the country that provide data to FDA's National Clearinghouse. Based on these reports, FDA estimates that 1.5 million cases (all ages) are being handled by the poison control center system in the United States. Many others are treated by private physicians and by those hospitals without poison centers. About 15,000 persons die from acute poisonings each year, although only about 1 percent are children under 5. (Adults generally are the ones who swallow the more toxic substances and in higher doses, primarily with suicidal intentions.)

What do young children get into the most? The most frequent culprits in 1979 were the same as the previous year: plants; soaps and detergents; antihistamines and cold medications; perfumes and colognes; and vitamins and minerals, primarily children's chewables. These products are common to most homes, and because many adults are unable to appreciate their potential to harm, they are often left where children can reach them.

Aspirin again was in sixth place and accounted for only 4 percent of the incidents involving children. Aspirin-related childhood deaths have declined from 140 per year in the 1940s due to changes such as child-resistant caps, voluntary limits by manufacturers on the contents of children's aspirin containers and improved medical care. Currently, 10 to 25 children die from aspirin poisoning annually, but experts believe that many of these deaths occur from therapeutic overdoses given by parents, instead of the actions of children. The decline is also due in part to greater use of aspirin substitutes which, correspondingly, are involved in more poisonings.

Some products are so hazardous that parents and other adults should make exceptional efforts to keep them out of reach of children. The 1979 case reports tell the story. Over 58 percent of the children who swallowed a popular brand of drain cleaner (Drano) containing lye showed evidence of injury, compared with 7 percent who ingested plant materials. A prescription anti-anxiety medication, Ativan, was close behind in injuries with a 50 percent toxicity case rate. Other products with high toxicity rates were Elavil (an anti-depressant drug), kerosene, Lomotil (anti-diarrhea), Easy Off Oven Cleaner, turpentine, Mellaril (an anti-psychotic drug), Thorazine (anti-psychotic) and ferrous sulfate (iron) diet supplements.

Adults are not always aware of the potential hazards of such products as iron supplements. An acute overdose of iron can result in corrosive damage to the stomach and small intestines, shock, cardiovascular collapse, damage to the liver and other organs and death. It can also cause permanent damage to the gastrointestinal tract and liver. Doses of 200 to 400 milligrams (mg) of iron have caused severe symptoms of injury in young children. This is equivalent to 14 to 27 children's vitamin-mineral supplements with iron (15 mg iron per tablet) or four to seven tablets of a typical adult iron supplement (60 mg per tablet, a common dosage for pregnant women). Iron supplements are found in every drugstore and are available without prescription in brightly colored tablets that may look like candy to a young child.

Tricyclic anti-depressants—so-called because of a three-ring chemical structure—are another special danger to children. These drugs are frequently prescribed to treat depressed adults. Furthermore, one formula is prescribed for children over 5 to help prevent bedwetting. Children have been known to take excessive doses in the belief that more of the medicine will produce better results. Even more common is accidental ingestion by a younger child of anti-depressants prescribed for adults or older brothers or sisters.

An overdose of a tricyclic anti-depressant can cause convulsions, coma, irregular heartbeat, a severe drop in blood pressure and depression of the respiratory system. Overdoses are frequently life-endangering and difficult to treat. For small children, one or two tablets containing 100 to 150 mg can be toxic. Doses for bedwetting are usually given in 25 mg tablets, hence eight to 12 tablets could be toxic.

Parents who are careful about handling or storage of poisonous substances are the first line of defense between children and poisons. To keep parents and others aware of the perils of accidental poisoning of children, health authorities have for the last 20 years designated the third week of March as National Poison Prevention Week (this year March 21–27). But parents should heed these suggestions the year around:

- Retain the safety caps that come on some non-prescription drugs and other substances, and on prescription drugs.
- Keep hazardous substances in their original containers. Never transfer them to a cup or beverage bottle that may cause a child to think they are edible or drinkable.
- Keep medicines apart from other household products since containers may look enough alike to be confused.
- Get rid of unused medicines and household products by emptying what's left down the drain (unless label instructions suggest other methods for discarding them).
- Get rid of prescription medicines as soon as the illness for which they were prescribed is over, or the prescribing regimen is completed.
- Never tell a child that medicine is candy or that it tastes like candy.
- Never take medicine in front of a small child; the youngster may try to imitate you some time when you are not there.
- Teach children not to eat or drink anything that has not been given to them by parents or others in authority.
- Educate children who are old enough to understand about the dangers of taking overdoses of medicine.
- As much as possible, keep house plants out of the reach of small children.
- Keep a one-ounce bottle of syrup of ipecac in your home (to induce vomiting), but do not use it unless directed to do so by a poison control center or a doctor.
- Keep the phone number of your local poison control center near the telephone in case of emergency.

For a listing of poison control centers in the United States, write to:

Division of Poison Control
Bureau of Drugs (Room 13–45)
5600 Fishers Lane
Rockville, Md. 20857

—Louise Fenner

Smelling Trouble

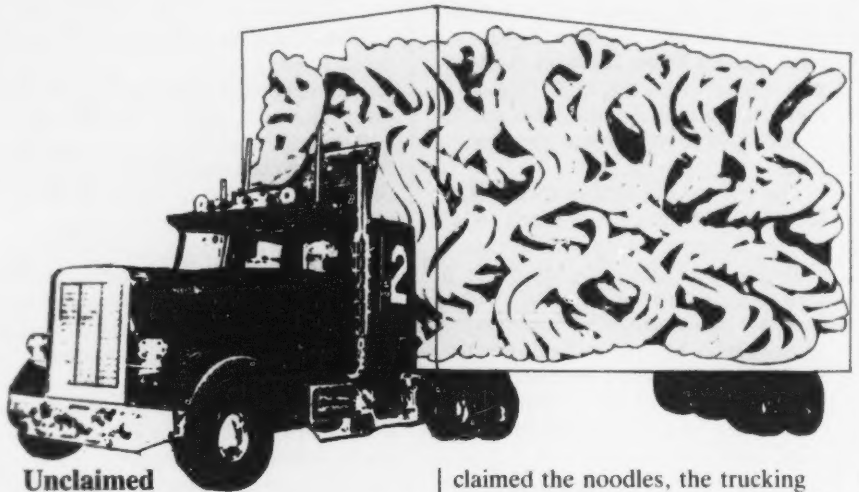
A soft drink bottling company in Waterloo, Iowa, had some area consumers wondering if it was selling thirst-quenchers or nose-pinchers.

The Pepsi-Cola Co. there recently received 25 complaints within three days about a foul odor from 16-ounce bottles of Pepsi-Cola. Although no illnesses were reported, the company did not immediately inform FDA of the incidents.

The tip-off for FDA's **St. Louis Station** came during a telephone conversation with FDA's Milwaukee resident post, which reported that a consumer complaint of a foul odor from a bottle of soft drink led to the inspection of a Milwaukee area Pepsi-Cola plant. The problem there had been traced to a contaminated supply of carbon dioxide and it was suggested that St. Louis personnel also inspect the Waterloo plant because both plants were supplied by the same industrial carbon dioxide manufacturer, Archer & Daniels of Illinois.

By the time St. Louis investigators got to the Waterloo plant, the company had traced the problem to carbonyl sulfide, a contaminant, in the carbon dioxide used in the product to make it bubbly. Company officials explained that when carbonyl sulfide reacts with water in carbonated soft drinks it produces hydrogen sulfide, which has the characteristic odor of rotten eggs and was responsible for causing the unpleasant odor reported by consumers.

Approximately 14,000 cases of the product had been manufactured with the contaminated carbon dioxide, but only 1,200 had been distributed. The company ultimately recovered about 705 cases and poured them down the drain.



Unclaimed

The manufacturer didn't want them; neither did the shipper or the distributor. So, when no one would accept two semi-trailer loads of packaged noodles, a Bryan, Ohio, trucking company called FDA's **Toledo resident post** for help.

The story began in Montebello, Calif., where Legend Enterprises, a food manufacturer, arranged to have a west coast trucking company deliver some goods in semi-trailers to a railroad for cross-country piggyback shipment to Chicago.

From Chicago the manufacturer arranged for two of the trailers, loaded with 12,416 cases of LaChoy noodles with beef or chicken packets, to be picked up by the Ohio trucking company and transported to LaChoy Food Products' distribution center in Archbold, Ohio.

When the shipment arrived at the distribution center, LaChoy refused to accept delivery when it found infestation by cockroaches in both trailers. Although the contamination occurred at some point between manufacture in California and Ohio, neither the processor nor the shipper would take responsibility. Since the LaChoy firm was not to blame, the shipment was returned to the trucking terminal.

When the manager of the trucking terminal called the resident post, FDA asked to examine the shipment. After FDA's laboratory examination of samples confirmed insect contamination, the agency's request for seizure was approved. Since no one claimed the noodles, the trucking company decided to have the goods destroyed. FDA investigators witnessed the burial of the noodles, estimated at $47,000, at a local landfill.

Hidden Sweets

Foods that contain sodium saccharin have long been required to show it on the label. Since 1978, labels of such foods have also been required to state that "Use of this product may be hazardous to your health. This product contains saccharin, which has been determined to cause cancer in laboratory animals."

Universal Protein Supplements Co. of Linden, N.J., used saccharin to sweeten its liquid protein supplement drinks, flavored with vanilla malt, chocolate, strawberry and banana, without declaring it on the label. One of Universal's competitors complained to FDA's **Newark District** office. This led to an FDA inspection of the firm and to seizure of 190 cases of the mislabeled Universal product, valued at $2,000.

Shortly after this, the firm was sold, with the seized goods still on the premises. The new owner, under FDA supervision, destroyed the entire lot.

Mercury No More

It took a year to do it, but the Globe Fish Co. of Boston, Mass., has been legally stopped from shipping swordfish containing hazardous levels of the heavy metal mercury.

Globe came to FDA's attention in July 1980, when the **New York Department of Agriculture and Markets** discovered 1.9 parts per million (ppm) of mercury in samples of swordfish shipped by Globe to a firm in Rochester. State officials wrote to the Rochester recipient firm and to Globe, reminding them that levels of mercury above 1 ppm in swordfish are illegal. They also shared their finding with FDA.

A month later, FDA and state investigators, sampling another Globe shipment to Rochester, again found mercury above the legal limit. The state embargoed the shipment, thus requiring that it be held undisturbed at the Rochester firm, while FDA obtained a court order for seizure. The lot was then destroyed under the supervision of a U.S. marshal.

Meanwhile Globe continued to ship swordfish to four New York firms, and state and FDA officials, taking samples at those firms, continued to find high levels of mercury ranging from 1.4 ppm to 1.94 ppm.

These lots, too, were seized and destroyed. But because of Globe's persistence, FDA decided that something more had to be done. The agency therefore asked the U.S. District Court of Massachusetts to enjoin Globe from entering in interstate commerce any swordfish containing mercury in excess of 1 ppm.

At a trial held in that court, experts described the effects on human health of mercury, among the most poisonous of the heavy metals, including the fact that it stays in body tissue and can cause brain damage, blindness and death. The court was convinced and on July 16, 1981—a year after the first swordfish seizure—issued the injunction against the company.

Soggy Sauce

An FDA inspector from the **Buffalo district** office, making a routine survey of orange juice production, noted 76 cases of jellied cranberry sauce pushed into a corner of the Great Northern Juice Corp. plant in Tonawanda, N.Y. The cases were wet through and the cans were rusty and leaking. Another 142 cases of the cranberry sauce were discovered in an unused truck trailer behind the plant. These also were wet, with some cans leaking and rusted. Quick examination showed 103 out of 288 cans were damaged or defective.

Checking lot numbers, the investigator found that the cranberry sauce had been manufactured by United Cranberry Growers in Hansen, Mass., in early 1976. It was purchased by the U.S. Department of Agriculture and shipped to the Great Northern plant, to be used in a lemon-berry drink in the USDA school lunch program in Buffalo.

The length of time—over four years—and the way in which it was stored by Great Northern contributed to the rusty, leaking condition of the 218 cases. According to FDA investigators, the results could have been harmful had the sauce been used as intended in the school lunch program.

FDA requested seizure of the cranberry sauce because it was unfit for food. The owners, Great Northern, made no attempt to claim the sauce, so the U.S. Court for the Western District of New York ordered it destroyed.

Bad Beef

State National Provision Co. of Albany, N.Y., recalled shipments of precooked (roast) beef from distributors in five northeastern states after tests by the **New York Department of Agriculture and Markets** found samples of the product contaminated by salmonella.

Students at a New York college had become ill after eating the beef, served in the school cafeteria. Their symptoms—nausea, headache and intestinal upset—indicated salmonella poisoning, the most common of the bacterial foodborne illnesses. Laboratory tests confirmed it. Salmonella contamination is usually caused by improper handling or preparation of food.

State National Provision distributes Orlev and State National brands of roast beef; it is sold to delicatessens, cafeterias and institutions.

It was one of several incidents of salmonellosis traced to commercially prepared roast beef that occurred in the eastern United States in 1981. An outbreak at a picnic and one at a neighborhood party were associated with meat prepared by Vincent Giodano Proscutto, a meat processor in Philadelphia. Another outbreak affecting 35 people occurred at a hospital in St. Albans, Vt. In the latter case, FDA's **Essex Junction resident post** worked with the U.S. Department of Agriculture and state and local officials to investigate the problem.

The federal government's Centers for Disease Control in Atlanta, which studies the patterns of such events, cautions that salmonella can thrive in various foods, including undercooked and rare roast beef. CDC advises persons who buy precooked beef to reheat it thoroughly (in effect, cook it again) after purchase. "Excessively rare" roast beef should not be eaten, CDC says.

Back to the Bay

After a brief interruption caused by a finding of high levels of fecal coliform bacteria in the company's oysters, Kennerly and Son, Nanticoke, Md., is again shipping raw oysters to Arizona.

Kennerly harvests oysters from beds in the lower Chesapeake Bay and apparently was working in a location that, unknown to the company, had become contaminated by sewage. This can happen when heavy rains wash down from populated areas into coastal waters of the bay and there is considerable water runoff into rivers that drain into the bay. It takes a week or so for the contaminated water to clear up, and until then no shellfish should be harvested.

The **Arizona Department of Health Services** found fecal coliform counts of 35,000 per grams of meat in oysters that Kennerly had shipped to Tucson and Phoenix. The maximum fecal coliform count set by FDA under the National Shellfish Sanitation Program is 230 per 100 grams of meat. Kennerly stopped working the contaminated beds until the waters tested clean, then resumed harvesting and shipping.

Coliform counts in shellfish can be high if the products are held too long and are not properly packed and refrigerated when shipped. Coliform bacteria grow rapidly, and freshly taken oysters with an initial low bacteria count may become unacceptable by the time they reach their destination, if not properly handled.

Gotcha!

When an Illinois drug company refused to permit an FDA inspection, an enterprising investigator got the information he wanted another way.

It was the third time investigators from the **Waukegan resident inspection post** had tried to make a follow-up inspection of KN Enterprises, Skokie, and had been refused. The company had signed a consent decree of permanent injunction agreeing not to manufacture or distribute contaminated drugs and to bring its operation into compliance with FDA regulations. The injunction was requested after investigators from FDA's Waukegan resident post reported a variety of problems including violations of good manufacturing practices, and samples of a bladder irrigation solution and an antibiotic solution, both labeled as being "sterile," were found contaminated by mold and bacteria.

When two Waukegan investigators returned to make sure the company was following the terms of the injunction, the company's president refused to allow them on the premises. A repeat attempt met with a similar refusal.

One of the investigators then made a third attempt to inspect the firm. He was again refused admittance, but happened to notice a UPS delivery truck making a visit to the company. The investigator questioned the driver, who reported that he had been making regular pick-ups from KN Enterprises and that some of the packages were addressed to hospitals. FDA traced shipments to two Wisconsin hospitals, which reported they had received the bladder irrigation solution during the period the injunction was in force.

FDA then obtained a court order to inspect KN Enterprises. The Waukegan investigators confirmed during this inspection that the firm had been shipping drugs and thus had violated the court injunction.

U.S. marshals seized three lots of the bladder irrigation solution, and KN Enterprises was fined $8,500 plus court costs.

—Compiled and written by Carol Ballentine, Richard Thompson and Michael Herndon.

Seizures and Postal Service Cases

FILED SEIZURE ACTIONS charge violations of the Federal Food, Drug, and Cosmetic Act and are initiated based upon FDA recommendations. A seizure action is commenced by the filing of a complaint in the U.S. district court where the goods are located. A U.S. marshal is then directed by the court to take possession of the goods, removing the product from commerce, until the matter is resolved.

A total of 12 actions to remove from the consumer market products charged to be violative was reported in September 1981. These actions included 8 seizures of foods: 4 involving charges concerning contamination and insanitary handling, and 4 involving charges concerning economic and labeling violations. Others included 4 of drugs (including 2 of veterinary).

PRODUCT, DISTRICT & DATE FILED	FIRM & PLACE OF BUSINESS	CHARGES
	FOOD/Contamination, Spoilage, Insanitary Handling	
Flour/U.S. District Court for the District of Puerto Rico 9/21/81	Borinquen Macaroni Corp./Yauco, P.R.	Product was held under insanitary conditions and contained rodent filth.
Flour/U.S. District Court for the Western District of New York 9/22/81	Barry Food Products, Inc./Buffalo, N.Y.	Product was held under insanitary conditions.
Halibut, frozen, dressed, headed/U.S. District Court for the Western District of Washington 9/11/81	Sitka Sound Seafoods/Sitka, Alaska	Product contained decomposed fish.
Pinto beans, dried/U.S. District Court for the Western District of Texas 6/19/81	Casso-Guerra & Co., Inc./Eagle Pass, Texas	Product was held under insanitary conditions.
	FOOD/Economic and Labeling Violations	
"COJM" mixes and "Sweetened O.J."/U.S. District Court for the Western District of Texas 7/14/81	Citrex, Inc./San Antonio, Texas	The valuable constituent orange juice has been omitted or abstracted from the articles and other substances have been substituted; the color turmeric has been added to the articles to make the foods appear better or of greater value than they are; the articles contain the non-conforming color additives turmeric and annatto since no regulation permits their addition to concentrated orange juice for manufacturing or to sweetened orange juice; the labeling of the "COJM" mixture is false and misleading as to the identity of the product since it is not concentrated orange juice for manufacturing; the articles fail to conform to the respective definitions and standards of identity for orange juice and concentrated orange juice for manufacturing due to added color and other specified substances; and the articles contain artificial coloring and their labels fail to state that fact.
"Maple" syrup, Wild Mountain brand/U.S. District Court for the Southern District of Mississippi 7/27/81	Paul Pilgrim Syrup Co./Dekalb, Miss.	Product represented as being maple syrup, but corn syrup has been substituted for maple syrup; labeling falsely represents the food to be maple syrup; article fails to conform to such definition and standard of identity for maple syrup since it contains corn syrup; and the article was in violation of the Fair Packaging and Labeling Act since the quantity of contents are expressed as "Net Wt. 3 Lbs. contents (32 Fl. Ozs.)" and "Net Wt. 1½ Lbs. contents (16 Fl. Ozs.)" instead of "1 Qt. (32 Fl. Ozs.)" and "1 Pt. (16 Fl. Ozs.)."
Protein supplement drink/U.S. District Court for the District of New Jersey 8/14/81	Universal Protein Supplements Corp./Linden, N.J.	Saccharin has been substituted for sugar; the ingredient saccharin is not declared on label; and the article's label does not bear the required hazard statement.

PRODUCT, DISTRICT & DATE FILED	FIRM & PLACE OF BUSINESS	CHARGES
"Sorghum" syrup/U.S. District Court for the Western District of Arkansas 9/18/81	Griffin Grocery Co./Muskogie, Okla.	Glucose syrup has been substituted for sorghum syrup; the article's labeling is false and misleading as to the article's identity since the article does not consist wholly of syrup from sorghum; the article's labeling is false and misleading as to the article being manufactured by Lemuel Roye Farms, Stigler, Okla.; the article fails to conform to the definition and standard of identity for sorghum syrup, and the article is in violation of the Fair Packaging and Labeling Act due to a non-conforming quantity of contents statement as to expression of weight, size of type, and spacing from other statements.
	DRUGS/Human Use	
Brompheniramine maleate & isoephedrine sulfate tablets/U.S. District Court for the Eastern District of Arkansas 7/28/81	Pharmadyne Laboratories, Inc./Elmwood Park, N.J.	Circumstances of manufacture not in conformity with current Good Manufacturing Practices.
Furosemide tablets/U.S. District Court for the Central District of California 7/14/81	Superpharm Corp./Central Islip, N.Y.	New drug without an effective approved New Drug Application.
Propap-100 brand of propoxyphene napsylate with acetaminophen/U.S. District Court for the Central District of California 6/5/81	Premo Pharmaceutical Laboratories, Inc./S. Hackensack, N.J.	Product is a new drug without an effective approved New Drug Application; product's labeling lacks adequate directions for use and is not exempted due to new drug status.
	DRUG/Veterinary	
Durvet Pink Eye spray/U.S. District Court for the Southern District of Illinois 7/15/81	Durvet, Inc., Chem-Tech, Ltd./Des Moines, Iowa	Product is a new animal drug and no approval of a New Animal Drug Application is in effect with respect to its use or intended use.

U.S. POSTAL SERVICE

actions taken in medical cases as authorized in the Mail Fraud Statute (18 U.S.C. 1341) and/or the False Representation Statute (39 U.S.C. 3005) as reported by the Chief Postal Inspector.

Complaints Filed by Law Department Under 39 U.S.C. 3005 (False Representation)

July 1, 1981: **Brant Pharmacal,** P.O. Box 992, Toledo, Ohio. Advertising and sale through the mail of "Stimulants." These stimulants are being sold as look-alike narcotics.

July 1, 1981: **Akers Pharmaceutical Inc.,** 325 Electric Ave., Lewistown, Pa. Advertising and sale through the mail of "Stimulants." These stimulants are being sold as look-alike narcotics.

July 6, 1981: **Cosvetic Labs,** P.O. Box 1097, Deerfield Beach, Fla. Advertising and sale through the mail of the product "Assist Appetite Control Plan," representing the ability to cause weight loss.

July 7, 1981: **Elda Originals,** Box 515, Second Ave., Highland Park, Ill. Advertising and sale through the mail of the product "Saunex Massage Cream." The ad states, in part, "massage this scientifically formulated cream for a minute into those parts of your body where you wish to streamline your figure. Saunex will help rid you of all the unsightly fat deposits which are likely to settle around your waist, upper arms, thighs, hips . . ."

July 8, 1981: **California Pacific Research, Inc.,** P.O. Box 2570, Sparks, Nev. Advertising and sale through the mail of the product "New Generation," representing the ability to "stop and reverse the effects of male pattern baldness. Existing hair will stop falling out."

July 8, 1981: **Joliesse,** 9025 Wilshire Blvd., Beverly Hills, Calif. Advertising and sale through the mail of the product "Joliesse Wrinkle Cream," representing the ability to "stimulate the growth of new skin! . . . Accelerate the skin renewal process and make you look years younger!"

July 8, 1981: **The Health Energetic Company,** 16783 Beach Blvd., Huntington Beach, Calif. Advertising and sale through the mail of the product "Hair Energetic," representing the ability to "reverse male patterned baldness."

July 8, 1981: **Collins Laboratories,** Box 60151, Oklahoma City, Okla. Advertising and sale through the mail of the product "Biotin," representing the ability to cure baldness.

July 13, 1981: **Paco,** P.O. Box 9504, Madison, Wis. Advertising and sale through the mail of the product "Potency Aids," representing the ability to cure "male impotences—causes, remedies."

July 21, 1981: **Future Research,** 492 Prospect Ave., West Orange, N.J. Advertising and sale through the mail of the product "Orbitrene Diet Pill." The ad states, in part, "Now, I guarantee that you will lose 79 pounds of ugly fat in 2 months! How easily the orbitrene method works to permanently control weight."

August 11, 1981: **Paul Andre, Ltd.,** 245 E. 25th St., New York, N.Y.

Complaints Filed by Law Department Under 39 U.S.C. 3005 (False Representation)

Advertising and sale through the mail of the product "Hollywood Skincare Program." The ad states, in part, "at last, a positive cure! . . . Complete disappearance of it . . . proof that cellulite can be beaten."

August 12, 1981: **Slim Suit,** 175 Fifth Ave., New York, N.Y. Advertising and sale through the mail of the product "Slim Suit," representing the ability to "lose weight while you sleep! Slim Suit, the sensational body trimmer, no exercise, no dieting, no drugs . . . quickly melts away excess weight and fluid without any effort on your part."

August 12, 1981: **Anaxo Labs,** Box 13731, Orlando, Fla. Advertising and sale through the mail of the product "Ana-Zyme." The ad states, in part, "temporary relief from arthritis and bursitis is great but . . . Ana-Zyme is better . . . has been called a true breakthrough."

August 17, 1981: **Conan Research,** P.O. Box 442, Twinsburg, Ohio. Advertising and sale through the mail of the product "Bio-Genesis," representing the ability "to promote growth of hair in male pattern baldness and as a remedy for loss of hair."

August 19, 1981: **Elda Originals,** Box 515, Second Ave., Highland Park, Ill. Advertising and sale through the mail of the product "Hypercrinal 444," representing the ability "to prevent balding . . . keeps hair healthy and grows long within the shortest time."

August 19, 1981: **Elda Originals,** Box 515, Second Ave., Highland Park, Ill. Advertising and sale through the mail of the product "Fulbloom Anti-Wrinkle Cream." The ad states, in part, "cares for and strengthens the skin and makes wrinkles disappear . . . anti-septic and anti-bacterial."

August 20, 1981: **American Medtech, Inc.,** 3659 India St., San Diego, Calif. Advertising and sale through the mail of the product "Pain Stop." The ad states, in part, "far superior to the regular line of liniments and associated products found in variety and drugstores across the country . . . new drug discovered for arthritis, fibrositis, rheumatism, FDA approved."

False Representation Orders Issued by Judicial Officer Under 39 U.S.C. 3005

June 2, 1981: Against **Sean Micheals** and **Sara Micheals,** 1200 66th St., North, St. Petersburg, Fla. Satisfactory evidence was presented to the Postal Service that Sean and Sara Micheals and their representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firms were advertising the products "Sean Micheals Bust Expander" and "Sara Micheals Protein for the Bust." The ads state, in part, "My breasts went from hopeless to fantastic in less than 15 days," and "in less than 15 days I went from tragic to terrific using the fantastic Sara Micheals Protein for the Bust."

July 7, 1981: Against **Capricorn Pharmaceuticals,** Box 15393, Chattanooga, Tenn. Satisfactory evidence was presented to the Postal Service that Capricorn Pharmaceuticals and their agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising "Stimulants." These stimulants are being sold as look-alike narcotics.

July 9, 1981: Against **The Source,** 1706 Central S.E., Albuquerque, N.M. Satisfactory evidence was presented to the Postal Service that The Source and their representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising "Stimulants." These stimulants are being sold as look-alike narcotics. The ad states, in part, "Like stimulation? Look inside. Legal stimulants at wholesale prices. No legal stimulants stronger than some prescription drugs pick-you-up and stimulate you."

July 16, 1981: Against **That Special Look, Inc.,** P.O. Box 1490, Pompano Beach, Fla. Satisfactory evidence was presented to the Postal Service that That Special Look, Inc., and their agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Slim-X," representing the ability to cause weight loss.

July 16, 1981: Against **C & C Vitamins & Sundries, Inc.,** P.O. Box 455, Pittsburgh, Pa. Satisfactory evidence was presented to the Postal Service that C & C Vitamins & Sundries, Inc., and their representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising "Stimulants." These stimulants are being sold as look-alike narcotics.

July 20, 1981: Against **McKenzie-Roberts,** Box 510028, Miami, Fla. Satisfactory evidence was presented to the Postal Service that McKenzie-Roberts and their representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Nilamine." The ad states, in part, "lose up to 60 lbs. in 12 short weeks!!! The Nilamine program does not let you starve yourself . . . can help you become trim and beautiful in the weeks to follow."

July 31, 1981: Against **Quest Research,** P.O. Box 9669, Atlanta, Ga. Satisfactory evidence was presented to the Postal Service that Quest Research and their agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Calorie Eliminator," representing the ability to "burn off more fat than if you ran 98 miles a week! Up to a full size smaller in just 5 days."

August 4, 1981: Against **Athena Products, Ltd.,** P.O. Box 81112, Chamblee, Ga. Satisfactory evidence was presented to the Postal Service that Athena Products, Ltd., and their representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the products "The Youth Factor, RNA, Eu-Zinc-D, Power Tabs, Chromill GTF, Natural Calm, Food for Thought, Rx for Aging, META-E, Ex-Sel, and Cellulite TR3." The published advertisements state, in part, "stay healthy, alert, energetic and young; helps slow the aging process; make your sexual relationship more exciting and satisfying than ever; increases your natural energy production; helps stabilize your blood sugar level; helps solve the problem of sleeplessness and nervousness; lets you improve your memory; help prevent and reverse the damage age does to skin; and cause weight loss."

August 4, 1981: Against **Athena Products, Ltd.,** 3545 Broad St., Chamblee, Ga. Satisfactory evidence was presented to the Postal Service that Athena Products, Ltd., and their agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Athena Stay Young Program," representing the ability to "slow down the aging processes. With regular use, the Athena Stay Young Program should result in skin that is moist and soft, higher energy levels, and a memory that will remain sharp."

August 4, 1981: Against **Athena Products, Ltd.,** P.O. Box 48392, Doraville, Ga. Satisfactory evidence was presented to the Postal Service that Athena Products, Ltd., and their representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Athena Nutrition for Women," representing the ability "to protect against the nutritional deficiencies that age women more quickly."

August 4, 1981: Against **Athena Products, Ltd.,** P.O. Box 80783, Atlanta, Ga. Satisfactory evidence was presented to the Postal Service that Athena Products, Ltd., and their agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Cellulite P.M.," representing the ability to "break up cellulite even while you sleep."

Notices of Judgment

NOTICES OF JUDGMENT on Seizure Actions

FOOD/Poisonous and Deleterious Substances

Alfalfa hay, baled, at Gravette, W. Dist. Ark.
Charged 6–4–81: when shipped by Max Hedges, Elk City, Kan., from Tonkawa, Okla., the article contained the pesticide chemical toxaphene in excess of the tolerance prescribed for alfalfa hay; 402(a)(2)(B). Default decree ordered destruction. (F.D.C. No. 63485; S. No. 81–221–982; N.J. No. 1)

FOOD/Contamination, Spoilage, Insanitary Handling

Candies, at North Augusta, Dist. S.C.
Charged 2–20–81: while held by Revco Drug Stores, Inc., North Augusta, S.C., the articles contained rodent filth and had been held under insanitary conditions; 402(a)(3) and (4). Default decree ordered the articles destroyed. (F.D.C. No. 63324A; S. No. 81–158–671; N.J. No. 2)

Cereal, breakfast, at Rochester, W. Dist. N.Y.
Charged 2–12–81: while held by Central Wholesale Grocery Corp., Rochester, N.Y., the article contained rodent filth and had been held under insanitary conditions; 402(a)(3) and (4). Default decree ordered destruction. (F.D.C. No. 63326; S. No. 81–252–106; N.J. No. 3)

Cornmeal, at Dallas, N. Dist. Texas.
Charged 1–26–81: while held by Fiesta Foods, Inc., Dallas, Texas, the article had been held under insanitary conditions; 402(a)(4). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63303; S. No. 81–266–321; N.J. No. 4)

Rice, at Lincoln, Dist. Neb.
Charged 6–24–81: while held by Kim Hinkley in a commercial van, Lincoln, Neb., the article contained rodent filth and had been held under insanitary conditions at his warehouse; 402(a)(3) and (4). Default decree ordered destruction. (F.D.C. No. 63497; S. Nos. 81–262–164/6; N.J. No. 5)

Shrimp, frozen, at Brooklyn, E. Dist. N.Y.
Charged 9–25–79: when shipped by Sunrise Foods Co., Kaohsiung, Taiwan, China, the article, which was under a U.S. Customs Service Transport and Export Permit and which was labeled in part "P&D Block Shrimps . . . Packed For: Intersea Fisheries Ltd. . . . Product of Taiwan," contained decomposed shrimp; 402(a)(3). Consent decree authorized release to Intersea Fisheries, Ltd., New York, N.Y., for re-export to Taiwan. (F.D.C. No. 62469; Import S. No. 255674; N.J. No. 6)

Sugar, at Boston, Dist. Mass.
Charged 5–11–81: while held by See Sun Ho Kee Co., Inc., Boston, Mass., the article contained rodent filth and had been held under insanitary conditions; 402(a)(3) and (4). Default decree ordered destruction. (F.D.C. No. 63462; S. No. 81–159–352; N.J. No. 7)

Whiskey, other liquor, beer, carbonated beverages, canned grapefruit juice, and **cherries,** at Nome, Dist. Alaska.
Charged 3–27–75: while held for sale, the articles had been held under insanitary conditions whereby they might have been contaminated with filth and whereby they might have been rendered injurious to health; 402(a)(4). The litigation in the district court is reported in N.J. No. 14 of the Nov. 1980 issue of *FDA Consumer*. The claimant (K & L Distributors, Inc., Nome, Alaska) appealed the court's decision upholding FDA's finding that the claimant's reconditioning method was not scientifically acceptable. The court of appeals affirmed the finding in favor of FDA, saying:

"K & L Distributors, Inc. brings this appeal from a judgment for the destruction of 1,638 cases of alcoholic beverages entered by the United States District Court for the District of Alaska under the authority of the Federal Food, Drug and Cosmetic Act (Act), 21 U.S.C. § 301 *et seq.* The district court stayed destruction of these articles pending appeal to this court. K & L asserts that the district court erred in ruling that appellant's method of reconditioning the articles must be rejected in favor of the method approved by the Food and Drug Administration (FDA). Appellant also suggests that reconditioned articles should be released from seizure on the basis of sampling and that administrative tolerances should be applied to determine if articles should be released from seizure.

"On November 11, 1974, a flood swept through the city of Nome, Alaska, caused by storm driven waves from the Bering Sea with the wind reaching speeds of 70 miles per hour. The flood waters caused extensive damage to the commercial district of Nome. Included in the commercial district is the Bering Sea Saloon, the location of the articles that are the subject of this controversy. The flood waters apparently burst through the back door of the saloon, resulting in merchandise being thrown to the ground and being exposed to various amounts of sea water.

"The flood also destroyed the city's sewage disposal plant. The raw untreated sewage effluent was dumped into the Snake River and it fanned out in all directions when it reached the Bering Sea. This situation continued for a period of between sixteen and eighteen hours. It is possible that the raw sewage was washed into the commercial district of Nome and into the Bering Sea Saloon by the waves. . . .

"On June 3, 1975 K & L consented to the condemnation and destruction of the beer and nonalcoholic articles of food. On June 9, 1976, K & L entered into another consent decree with respect to the cases of alcohol. First, K & L admitted that the articles under seizure were adulterated in violation of 21 U.S.C. § 342(a)(4). They were therefore condemned pursuant to 21 U.S.C. § 334(a). Second, the consent decree provided that the goods were to be released from custody for the purpose of reconditioning the articles pursuant to 21 U.S.C. § 334(d) under the supervision of the FDA. Because the alcohol may have been contaminated by raw sewage, the FDA would only approve a reconditioning plan that included redistillation of the alcohol. Appellant claimed that this plan would be economically disastrous and brought an action seeking approval and implementation of its reconditioning plan. The district court approved the FDA's plan. Appellant's Motion to Permit Reconditioning After Decree of Condemnation and Motion for Reconsideration were both rejected. The district court then ordered the condemned articles destroyed but stayed the order during the pendency of this appeal.

"K & L initially contends that the owner of seized goods should have the right to choose the method of reconditioning that is to be used to bring adulterated articles in compliance with the Act. In assessing this claim, we must first examine the statutory framework surrounding this type of situation. Section 334(a)(1) of the Act allows a district court to condemn any article that is adulterated while held for sale after shipment in interstate commerce. A product is 'adulterated' if it has been 'held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health.' 21 U.S.C. § 342(a)(4). After it is determined that an article is 'adulterated,' it is subject to seizure pursuant to an arrest warrant. 21 U.S.C. § 334(b). The article is then disposed of by destruction or sale unless, upon payment of the costs of the proceeding and execution of a sufficient bond, the court orders the articles to be delivered to the owner to be destroyed or brought into compliance with the provisions of the Act under the supervision of an officer designated by the Secretary of Health, Education and Welfare. 21 U.S.C. § 334(d)(1).

"K & L admitted in the consent decree that the articles were adulterated. The consent decree provided that they were to be returned to K & L to be reconditioned under the supervision of the FDA. The only remaining question then is whether 'under the supervision of' the FDA requires appellant to adopt the FDA's recommended method of reconditioning the articles. K & L suggested a plan of reconditioning that included a soap and water washing of the bottles followed by a hypochlorite dip. Evidence existed which indicates that the bottles had been submerged in the seawater long enough to cause destruction of labels and stamps, leaking closures, and sediment and silt deposited on the neck, shoulder, and body of the bottles. There was also an indication that filth might be lodged between the caps and lips of the bottle. K & L's proposal was found unacceptable because it would not solve the problem of the filth under the caps. If a cap was removed for additional cleaning, there would be further contamination. Therefore, the FDA provided that the only acceptable method for remedying the insanitary condition would be through a complete reprocessing of the product by redistillation.

"It is the duty of the FDA to protect the health and welfare of the general public. . . . Therefore, the courts that have dealt with the issue presented in this case have held that it is proper to rely on the scientific expertise of the FDA in determining the acceptability of a reconditioning proposal and to require FDA approval of a reconditioning plan. *United States* v. *Allan Drug Co.*, 357 F.2d 713 (10th Cir.), cert. denied, 385 U.S. 899, 87 S.Ct. 203, 17 L.Ed.2d 131 (1966); *United States* v. *1,322 Cans, More or Less, of Black Raspberry Puree*, 68 F.Supp. 881 (N.D. Ohio 1946). In *Allan*, the Tenth Circuit addressed the meaning of the language of § 334(d)(1) as it applies to misbranded drugs. The court stated that once a district court delivers a misbranded (or adulterated) article to the owner to bring it into compliance with the law under the supervision of an officer designated by the Secretary of HEW, 'the supervisory powers committed to the Secretary undoubtedly carry broad authority to determine whether and in what manner the labeling may be brought within compliance with the act. The judicial function is concerned with the end product of the labeling process. While the final decision lies with the courts, great weight must be given to the administrative decision.' 357 F.2d at 719. The district court in *1,322 Cans* reached a similar conclusion with respect to articles of adulterated food when it stated that 'The Food and Drug Administration has determined that distillation is the only process which would recondition this puree for human consumption and which it would approve. I see no abuse of discretion in making this determination. To interfere would be substituting the judgment of the court for that of the Food and Drug Administration upon a matter which is better able to decide upon an issue which I think is not properly joined in this case.' 68 F.Supp. at 881.

"The district court properly deferred to the expertise of the FDA. While this court is not bound by *Allan* or *1,322 Cans*, we choose to follow the reasoning of those cases. A district court may rely on and give great weight to the FDA's finding that a reconditioning plan is not scientifically acceptable. The FDA did not abuse its discretion, even in light of the economic hardship imposed on appellants by its reconditioning plan. The district court, in its discretion, properly adopted the determination of the FDA.

"Because we have already determined that the district court properly adopted the FDA's procedure, we need not address appellant's contention concerning sampling and its suggestion concerning the adoption of administrative tolerance levels." (F.D.C. No. 60243; S. No. 19-601H; N.J. No. 8)

FOOD/Economic and Labeling Violations

Shrimp, canned, at Yakima, E. Dist. Wash.

Charged 6-26-81: while held for sale after being repackaged locally, the article, labeled in part "Icy Point Tiny Broken Shrimp . . . Distributed By New England Fish Co. Seattle, Wash.," was short weight; the article failed to conform to the standard of fill of container for canned shrimp, since the cut out weight of shrimp taken from a number of containers was less than 60 percent of the weight of water required to fill the container; 403(e)(2), 403(h)(2). Default decree ordered destruction. (F.D.C. No. 63481; S. No. 81-241-196; N.J. No. 9)

COLOR ADDITIVES

Guava shells, canned, two seizure actions, at Miami, S. Dist. Fla., and Tampa, M. Dist. Fla.

Charged 9-10-79 and 10-26-79: when shipped by Loma Linda, S.A., San Juan del Rio, Mexico, the articles, labeled in part "Ancel Guava Shells In Sugar Syrup Net Wt. 16 [or "30"] Oz. (1 Pound [or "1 Pound 14 oz"]) Packed For Ancel Products, Inc., Miami, Florida . . . Product of Mexico," contained the non-conforming color additives External D and C Red Number 10 and Color Index 16255; 402(c). The articles were claimed by the shipper. Upon stipulation of the parties, the Tampa action was consolidated with the Miami action.

The government moved for summary judgment. The court granted the government's motion for summary judgment and ordered the articles destroyed. (F.D.C. Nos. 62438 and 62451; S. Nos. 79-193-305/6 and 79-167-221/2; N.J. No. 10)

DRUGS/Human Use

Acetaminophen tablets, elixir terpin hydrate & codeine, phenolated calamine lotion, zinc oxide ointment, and **other stocks of finished drugs, in-process drugs and drug components,** at Philadelphia, E. Dist. Pa.

Charged 3-24-80 and amended 3-25-80: while held by Hance Brothers & White Co., Inc., Philadelphia, Pa., the circumstances used for the manufacture, processing, packing and/or holding of the articles failed to conform with current good manufacturing practices; 501(a)(2)(B).

The articles were claimed by the dealer. Subsequently, a number of drugs which had been seized at the dealer's premises but which were not owned, manufactured, processed, packed or held by the dealer were released. Consent decree authorized release of the remaining drug stocks to the claimant for salvaging. (F.D.C. No. 62908; S. No. 79-144-715 et al.; N.J. No. 11)

Allopurinol tablets, at North Hollywood, C. Dist. Calif.

Charged 2-13-80: when shipped by Pharmadyne Laboratories, Inc., Elmwood Park, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). The article was claimed by the shipper. Pursuant to stipulation, the action was transferred to the District of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the article destroyed. (F.D.C. No. 62819D; S. No. 80-208-582; N.J. No. 12)

Allopurinol tablets, at Brooklyn, E. Dist. N.Y.

Charged 6-11-79: when shipped by Pharmadyne Laboratories, Inc., Hackensack, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). The article was claimed by the shipper. Pursuant to stipulation, the action was consolidated for trial in the District of New Jersey. Subsequently, a consent decree ordered destruction. (F.D.C. No. 62296; S. No. 79-161-827 et al.; N.J. No. 13)

Allopurinol tablets, at Tacoma, W. Dist. Wash.

Charged 5-8-79: when shipped by Pharmadyne Laboratories, Inc., Hackensack, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). The article was claimed by the shipper. Pursuant to stipulation, the action was transferred to the Eastern District of New York for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the article destroyed. (F.D.C. No. 62250; S. No. 79-176-721; N.J. No. 14)

Allopurinol tablets, chlorthalidone tablets, diethylpropion HCl tablets, doxylamine succinate with B_6 tablets, hydroxyzine HCl tablets, trisulfamethoxazole tablets, and trimethoprim with sulfamethoxazole tablets, at Valley Stream, E. Dist. N.Y.
Charged 2-7-80: when shipped by Pharmadyne Laboratories, Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the District of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62777; S. No. 80-200-690; N.J. No. 15)

Allopurinol tablets, diethylpropion HCl tablets, and **furosemide tablets,** at Mechanicsville, N. Dist. Iowa.
Charged 1-28-80: when shipped by Pharmadyne Laboratories, Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Subsequently, a consent decree ordered destruction. (F.D.C. No. 62796; S. No. 80-208-560; N.J. No. 16)

Allopurinol tablets, diethylpropion HCl tablets, doxylamine succinate tablets, furosemide tablets, hydroxyzine HCl tablets, hydroxyzine pamoate capsules, prochlorperazine capsules, trimethoprim with sulfamethoxazole tablets, and **chlorthalidone tablets,** at Rockville Center, E. Dist. N.Y.
Charged 2-8-80: when shipped by Pharmadyne Laboratories, Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the District of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62776; S. No. 80-200-691 et al.; N.J. No. 17)

Chlorthalidone tablets, allopurinol tablets, prochlorperazine tablets, and **hydroxyzine pamoate capsules,** at Madison Heights, E. Dist. Mich.
Charged 3-3-80: when shipped by Pharmadyne Laboratories, Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the District of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62770; S. No. 80-183-482; N.J. No. 18)

Chlorthalidone tablets, and **furosemide tablets,** at St. Louis, E. Dist. Mo.
Charged 2-1-80: when shipped by Pharmadyne Laboratories, Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the Eastern District of New York for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62820; S. No. 80-208-581; N.J. No. 19)

Chlorthalidone tablets, furosemide tablets, hydroxyzine HCl tablets, hydroxyzine pamoate capsules, allopurinol tablets, diethylpropion HCl tablets, doxylamine succinate with B-6 tablets, and **trimethoprim with sulfamethoxazole tablets,** at Brooklyn, E. Dist. N.Y.
Charged 1-24-80: when shipped by Pharmadyne Laboratories, Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the District of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62753; S. No. 80-200-046; N.J. No. 20)

Chlorthalidone tablets and **hydroxyzine HCl tablets,** at Tucson, Dist. Ariz.
Charged 2-5-80: when shipped by Pharmadyne Laboratories, Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a).The articles were claimed by the shipper. Consent decree ordered destruction. (F.D.C. No. 62799; S. No. 80-208-566; N.J. No. 21)

Diethylpropion HCl tablets, at North Hollywood, C. Dist. Calif.
Charged 2-13-80: when shipped by Pharmadyne Laboratories, Inc., Elmwood Park, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). The article was claimed by the shipper. Pursuant to stipulation, the action was ordered transferred to the District of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the article destroyed. (F.D.C. No. 62819C; S. No. 80-208-582; N.J. No. 22)

Diethylpropion HCl tablets, at City of Commerce, C. Dist. Calif.
Charged 6-16-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (F.D.C. No. 63061; S. No. 80-245-421; N.J. No. 23)

Diethylpropion HCl tablets, at New Britain, Dist., Conn.
Charged 12-1-78: when shipped by Pharmadyne Laboratories, Inc., Hackensack, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). The article was claimed by the shipper. Pursuant to stipulation, the action was transferred to the Eastern District of New York for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the article destroyed. (F.D.C. No. 61975; S. No. 79-160-425; N.J. No. 24)

Diethylpropion HCl tablets, furosemide tablets, and **chlorothiazide with reserpine tablets,** at Brooklyn, E. Dist. N.Y.
Charged 3-28-79: when shipped by Pharmadyne Laboratories, Inc., Hackensack, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a).The shipper claimed the articles. Pursuant to stipulation, the action was consolidated for trial in the District of New Jersey. Subsequently, a consent decree ordered destruction. (F.D.C. No. 62204; S. No. 79-161-663; N.J. No. 25)

Diethylpropion HCl tablets and **other specified drugs,** at San Diego, S. Dist. Calif.
Charged 4-18-79: when shipped by Pharmadyne Laboratories, Inc., Hackensack, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a).The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the District of New York for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the article destroyed. (F.D.C. No. 62202; S. No. 79-154-252; N.J. No. 26)

Doxylamine succinate with B-6 tablets, at City of Commerce, C. Dist. Calif.
Charged 6-13-80: when shipped by Pharmadyne Laboratories, Inc., Elmwood Park, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (F.D.C. No. 63056; S. No. 80-245-421; N.J. No. 27)

Furosemide tablets, at Baltimore, Dist. Md.
Charged 2-8-80: when shipped by Pharmadyne Laboratories, Inc.,

Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the District of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62782; S. No. 80–208–544; N.J. No. 28)

Furosemide tablets, at Salt Lake City, Dist. Utah.
Charged 3–10–79: when shipped by Pharmadyne Laboratories, Inc., Hackensack, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). The article was claimed by the shipper. Pursuant to stipulation, the action was transferred to the Eastern District of New York for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the article destroyed. (F.D.C. No. 62209; S. No. 79–118–057; N.J. No. 29)

Furosemide tablets, at Oklahoma City, W. Dist. Okla.
Charged 7–29–80: when shipped by Generix Drug Corp., Hollywood, Fla., the article was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (F.D.C. No. 63124; S. No. 80–265–414; N.J. No. 30)

Furosemide tablets, and **diethylpropion HCl tablets,** at Hollywood, S. Dist. Fla.
Charged 12–13–78: when shipped by Pharmadyne Laboratories, Inc., Hackensack, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the Eastern District of New York for trial with a similar action. Subsequently, a consent decree ordered the articles destroyed. (F.D.C. No. 61989; S. Nos. 79–141–835/6; N.J. No. 31)

Furosemide tablets, and **other specified drugs,** at Cleveland, N. Dist. Ohio.
Charged 2–4–80: when shipped by Pharmadyne Laboratories, Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the District of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62792; S. No. 80–208–555; N.J. No. 32)

Hydroxyzine HCl tablets, and **hydroxyzine pamoate capsules,** at Royal Oak, E. Dist. Mich.
Charged 10–9–79: when shipped by Pharmadyne Laboratories, Inc., Hackensack, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the Eastern District of New York for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62555; S. No. 79–185–468 et al.; N.J. No. 33)

Hydroxyzine HCl tablets, diethylpropion tablets, hydroxyzine pamoate capsules, prochlorperazine capsules, spironolactone with hydrochlorothiazide tablets, trimethoprim with sulfamethoxazole tablets, and **chlorothiazide with reserpine tablets,** at Brooklyn, E. Dist. N.Y.
Charged 2–6–80: when shipped by Pharmadyne Laboratories, Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the District of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62769; S. No. 80–200–047 et al.; N.J. No. 34)

Hydroxyzine HCl tablets, hydroxyzine pamoate capsules, prochlorperazine capsules, spironolactone tablets, furosemide tablets, and **trimethoprim with sulfamethoxazole tablets,** at Baltimore, Dist. Md.
Charged 2–8–80: when shipped by Pharmadyne Laboratories, Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the District of New Jersey for consolidation for trial. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62786; S. No. 80–208–548; N.J. No. 35)

Hydroxyzine HCl tablets, and **chlorthalidone tablets, at** Wilmington, Dist. Del.
Charged 1–23–80: when shipped by Pharmadyne Laboratories, Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was consolidated for trial in the District of New Jersey. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62761; S. No. 80–230–992; N.J. No. 36)

Penicillin V potassium for oral solution (125 mg and 250 mg lots), at Baltimore, Dist. Md.
Charged 2–27–78: when returned from Detroit, Mich., to John D. Copanos & Sons, Inc., Baltimore, Md., the articles, which were labeled in part "Penapar VK (Penicillin V Potassium For Oral Solution) . . . 125 MG [or "250 MG"] Per 5 ML . . . Parke-Davis . . . Expiration Date: Oct. 1978," were from a batch of penicillin for which no antibiotic certificate, release or exemption was in effect; 502(l).

The article was claimed by John D. Copanos & Sons, Inc., Baltimore, Md., who denied the charge and alleged that a valid exemption was in effect for the claimant as a manufacturer. After discovery proceedings, the claimant moved to withdraw its claim without incurring costs or further charges, saying: 1. that the government's purpose in this action was to effect the destruction of the article; 2. that this proceeding had imposed financial hardship upon the claimant; 3. that the claimant had sought permission to donate the article to charity in a foreign country (all tests demonstrating that the article remained in a stable and sound condition); 4. that administrative and litigative delays by the government, over almost two years, had caused the designated lifespan of the article to near its end; and 5. that the government's action had been arbitrary and was contrary to its duties and general obligation of fairness, as follows: A. the proceeding was directed to accomplish the destruction of the article and to sanction the claimant for alleged failure to effect the destruction of the article; B. that the article had been shipped to Detroit, Mich., without seizure or other objection and shipped back to Baltimore, Md., with the approval and direction of the government; C. that the article was shipped when either a valid exemption by the claimant or Parke-Davis & Co. were in effect, and, even if no exemption was in effect, seizure was not warranted and no other seizure under such circumstances was remembered; D. that FDA had issued to the claimant a "Regulatory Letter," and only, upon receiving the claimant's objections, sought to establish authority for such "Regulatory Letters;" E. that FDA refused to consider certification of the article on the ground that the penicillin had been stored "under unknown conditions" in Singapore for many months, although claimant understood, FDA made no genuine inquiry as to the circumstances of storage in Singapore; and F. that claimant conducted negotiations to reach an amicable settlement but the position of the government made such settlement impossible.

The government opposed the claimant's motion to withdraw its claim, opposing the claimant's allegations of bad faith, but not opposing the motion for withdrawal of claimant's claim as long as court costs, costs of destruction and cost of supervision of destruction were borne by the claimant. The court rejected the claimant's arguments and favored the government's position, saying:

"The sole issue remaining in the case involves costs. Both parties agree that destruction of the subject articles should be effected. Under 21 U.S.C. §334(d), a condemnation decree is required before the articles can be destroyed. See *United States* v. *38 Cases, etc., Mr. Enzyme,* 369 F.2d 399, 400 (3d Cir. 1966). The United States contends that under 21 U.S.C. §334(e), the court costs, cost of destruction and cost of supervision of destruction should be borne by Copanos. Copanos disagrees, believing it inappropriate to subject it to the payment of costs as well as the destruction of the drugs.

"The statutory section at issue, 21 U.S.C. §334(e), provides as follows: '(e) When a decree of condemnation is entered against the article, court costs and fees, and storage and other proper expenses, shall be awarded against the person, if any, intervening as claimant of the article.'

"Copanos contends that this section is inapplicable if it is allowed to withdraw its claim. Its reasoning is that §334(e) only applies to a party who is still in the case as a claimant at the time the decree of condemnation is entered. Thus, if Copanos were allowed to withdraw before the decree was entered, §334(e) would not authorize an award of costs against it, because Copanos would no longer be a claimant at the time of the decree.

"The court disagrees with Copanos' argument because it is based upon an incorrect reading of §334(e). The statute does not provide for the payment of costs only after the decree of condemnation and only by the party *then* intervening as claimant. It is true that the award of costs is to be made at the time the decree of condemnation is entered. However, the statute mandates an award of costs against any person intervening as claimant in the proceeding; there is no requirement expressed in §334(e) that the person against whom costs are awarded still be a party to the proceedings at the time the decree is entered. The interpretation suggested by Copanos would allow an unsuccessful claimant to avoid the award of costs under §334(e) by merely withdrawing its claim prior to the entry of the condemnation decree. The court concludes that §334(e) requires an award of costs against a claimant even if that claimant attempts to withdraw prior to the decree. Since Copanos has unsuccessfully intervened as a claimant, costs should be awarded against it when the decree of condemnation is entered.

"Even if Copanos' interpretation of §334(e) was correct, an award of costs against it would still be proper since at this juncture in the proceeding a decree of condemnation should be entered. There is no longer any dispute concerning condemnation and destruction of the drugs; the only remaining question involves the award of costs. For all practical purposes, this case is now finished, and the preparation and entry of a decree of condemnation would seem appropriate. Therefore, the United States is requested to prepare a decree of condemnation." (F.D.C. No. 61614; S. No. 77-01-003; N.J. No. 37)

Trimethoprim with sulfamethoxazole tablets, at City of Commerce, C. Dist. Calif.
Charged 6-16-80: when shipped by Pharmadyne Laboratories, Inc., Elmwood Park, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (F.D.C. No. 63060; S. No. 80-245-421; N.J. No. 38)

DRUGS/Veterinary

Copper napthenate combination, at Columbus, S. Dist. Ohio.
Charged 6-10-81: when shipped by Harford Veterinary Supply Co., Darlington, Md., the article, labeled in part "Butler Fungitox . . . Copper Napthenate . . . Manufactured for: The Butler Company, Columbus, Ohio," was a new animal drug and no approval of a New Animal Drug Application was in effect with respect to the article's use or intended use; 501(a)(5). Default decree ordered destruction. (F.D.C. No. 63473; S. No. 81-272-791; N.J. No. 39)

MEDICAL DEVICES

X-ray system, Traceray IV, at Stockton, E. Dist. Calif.
Charged 10-10-79: the article, which had been manufactured by Western States Supply, Ltd., Pueblo, Colo., was dangerous to health when used as directed, because the article would emit radiation beyond the pre-set exposure time—502(j); the accompanying labeling was false and misleading in claiming compliance with the regulations' standards and in claiming that the devices would deliver the radiation exposure stated in the instruction manual—502(a); and the article's quality fell below its purported quality—501(c). Consent decree authorized release to the possessor for reconditioning. (F.D.C. No. 62570; S. No. 79-150-478; N.J. No. 40)

X-ray systems, Traceray III, six seizure actions, at St. Petersburg, M. Dist. Fla., Ft. Lauderdale, S. Dist. Fla., Sandy, Dist. Utah, Jonesboro, E. Dist. Ark., and Puyallup, W. Dist. Wash.
Charged 10-12-79, 10-12-79, 10-10-79, 10-4-79, 10-29-79, 10-16-79: the articles, which had been manufactured by Western States Supply, Ltd., Pueblo, Colo., were dangerous to health when used as directed, because the devices would emit radiation beyond the pre-set exposure time—502(j); the accompanying labeling was false and misleading in claiming compliance with the regulations' standards, and in claiming that the devices would deliver the radiation exposure stated in the instruction manual—502(a); and the articles' quality fell below their purported quality—501(c). Consent decrees authorized release to owners/possessors for reconditioning. (F.D.C. Nos. 62492, 62493, 62521, 62524, 62528, 62561; S. Nos. 79-166-341, 79-166-342, 79-193-808, 79-118-859, 79-137-505, 79-152-954; N.J. No. 41)

NOTICES OF JUDGMENT on Criminal Actions

Henry W. Borrego, president of Variety Seafoods, Inc., Tampa, M. Dist. Fla.
Charged 3-4-81: when shipped to Mobile, Ala., frozen raw breaded shrimp, labeled in part "Ocean Supreme 21 Shrimp In A Basket Packed By Variety Frozen Foods, Tampa, Florida," failed to conform to the definition and standard of identity, since the frozen raw breaded shrimp tested as less than 50 percent shrimp; 403(g). Guilty plea; $1,000 fine. (F.D.C. No. 61707; S. No. 77-91-966 et al.; N.J. No. 42)

Variety Seafoods, Inc. (formerly Variety Frozen Foods, Inc.), Tampa, M. Dist. Fla.
Charged 3-4-81: when shipped to Mobile, Ala., with intent to defraud and mislead, frozen raw breaded shrimp, labeled in part "Ocean Supreme 21 Shrimp In A Basket Packed By Variety Frozen Foods, Tampa, Florida," failed to conform to the definition and standard of identity, since the frozen raw breaded shrimp tested as less than 50 percent shrimp; 403(g). Guilty plea; $10,000 fine. (F.D.C. No. 61707; S. No. 77-91-966 et al.; N.J. No. 43)

NOTICES OF JUDGMENT on Injunction Actions

Cargill, Inc., South Carolina Farm Bureau Marketing Assn., James M. DeVeau, association general manager, and **Peter Reed,** corporation branch manager, North Charleston, Dist. S.C.
Charged 11-18-77 in a complaint for injunction: that the defendants at a grain storage facility at Pier #18, North Charleston, S.C., were

engaged in receiving, storing and exporting shelled corn; that FDA samples from corn stored in Pier #18 bins and corn exported by the defendants, established that some of such corn contained the added poisonous and deleterious substance aflatoxin in excess of 20 ppb; that more than 20 ppb of aflatoxin may be injurious to health; that, when such corn was exported, the exported corn did not conform to all of the provisions for exemption, due to the absence of documentation establishing: (a) that the corn was not in conflict with the laws of the countries to which it was intended for export, and (b) that the corn accorded to the specification of the foreign purchaser; and that the defendants had been advised on a number of occasions that their shelled corn contained amounts of aflatoxin in excess of the maximum level allowed by law; 402(a)(1); 801(d)(1).

The court issued a temporary restraining order which temporarily restrained and enjoined the complained of violations. A consent decree of preliminary injunction was subsequently entered into which continued to enjoin the complained of violations and which imposed a number of specified conditions on the defendants' operations, but which permitted certain intrastate sale of corn which had not entered interstate commerce under specified conditions. (Inj. No. 812; S. No. 77-29-868 et al.; N.J. No. 44)

Nova Scotia Food Products Corp., David Sklar, president, and **Emanuel Sklar,** vice president and treasurer, Brooklyn, E. Dist. N.Y.

Charged 4–7–76 in a complaint for injunction: that the defendants, at their Brooklyn, N.Y., plant, were engaged in manufacturing, processing, packing, holding and distributing hot-process smoked fish held for sale after interstate shipment; that FDA inspections revealed that the circumstances of manufacture, processing, packing and holding fish (other than chubs) failed to conform with the current good manufacturing practice regulations [21 CFR 1282.1–128(a)(7)], so as to produce for human consumption hot-process smoked fish under sanitary conditions which are adequate to prevent the formation of *Clostridium botulinum* type E toxin, a dangerous and frequently fatal substance; that the deviations from current good manufacturing practice regulations were illustrated by a number of specified FDA inspectional observations (including the heating, cooking and smoking of hot-process white fish at temperatures lower than required and less water-phase salt after brining than required); that FDA analyses of samples of the defendants' hot-process smoked white fish revealed a number of water-phase salt percentages ranging from 1.2 to 3.2 percent and averaging between 1.7 percent and 2.7 percent; and that the defendants were well aware that their activities were in violation of the law; 402(a)(4).

The court denied the government's request for a temporary restraining order. The government moved for preliminary permanent injunctions and such motions were consolidated for trial. After a trial before the court, the court found for the government, saying:

"Defendants are engaged in Brooklyn in the business of receiving in interstate commerce frozen or iced white fish which are processed by defendants, that is, they are brined, smoked and cooked. The white fish are then held for distribution and distributed to stores as smoked white fish. The Food and Drug Administration inspectors made inspections of defendants' plant in July 1975 and again in February 1976, and on each occasion they found that defendants were not processing the smoked white fish in accordance with the regulations, primarily in that the process did not meet the heat and brining requirements of 21 C.F.R. §128a.7(c)(4), (d)(2). Specifically the regulations required oven 'cooking' the white fish at 180° F. for 30 minutes if the salinity of the fish was at 3.5% or at 150° F. for 30 minutes if the salinity was at 5%. There is no real dispute as to the facts of defendants' practice. The defendants did not heat the fish at 180° F. for a half hour nor did the salinity of the fish reach the 3.5% level.

"The Current Good Manufacturing Practice (sanitation) regulations, dated November 2, 1970 and filed on November 12, 1970 for publication in the *Federal Register* of November 13, 1970 are not limited to salinity and temperature requirements. They include regulations with respect to unloading platform material and drainage; the provision of separate rooms for receiving and shipping, storing fish, pre-smoking operations including thawing, dressing and brining, and drying and smoking; the processes of packing and storage of the final product were to be carried out in separate rooms or facilities. There is a general requirement that the product be so processed as to prevent contamination by exposure to areas involved in earlier processing steps, to refuse, or to other objectionable areas. The regulations include equipment and utensil requirements with reference particularly to their being made of readily cleanable materials if they come into contact with the food products. The regulations require that adequate hand washing and sanitizing facilities be located in the processing room or rooms or in an area easily accessible from them; signs are to be provided directing employees to wash and sanitize their hands after each absence from their duty posts. There is provision for periodical removal of offal, and requiring that offal, debris, or refuse must not be accumulated in or about the plant. Each day the utensils and product-contact surfaces of equipment must be rinsed and sanitized, and fish containers are not to be nested or handled during processing in a manner conducive to contamination. The cleaning and sanitizing of utensils and equipment are to be so carried out so as not to lead to contamination of the product. Fish are to be adequately inspected and only clean, wholesome fish are to be processed. Time and temperature controls are established with respect to refrigerating, thawing, spraying and washing fish. Fish are to be completely eviscerated with the minimum disturbance of intestinal tract and thoroughly washed by a continuous spray system. The fish are to be brined in a solution that does not exceed 38° F. and the finished product is required to be cooled to 50° F. within 3 hours of cooking and to 38° F. or less within 12 hours after cooking. The finished product is to be handled only with clean, sanitized hands, gloves or utensils. Shipping containers are to indicate the perishable nature of the product and to specify that the fish must be shipped, stored and held for sale at 38° F. or less until consumed. The product is required to be coded so that each lot's processing history can be traced. Other sections of the regulations require indicating thermometers on freezer and cold storage elements and require a point-sensitive, continuous temperature-recording device to monitor both the internal temperature of the fish and the ambient temperature inside the processing oven, each recording device record to be identified as to specific oven load and date processed.

"The regulations thus closely supervise the handling of the fish not only by covering the processing procedures but also by setting requirements for equipment, general procedures and plant cleanliness.

"The inspections of July 1975 and February 1976 not only demonstrated failure to comply with the time and temperature and brining exactions of the regulations, but also revealed a failure to maintain the presmoking brining stage at the requisite low temperature and failure to achieve the requisite post-smoking and cooking temperature levels. The inspections at the defendants' plant disclosed further that it did not have all of the required indicating thermometers and temperature recording devices.

"As already indicated, there is no claim of compliance with the regulations. The defendants have not in any substantial way contested the findings of the FDA inspectors and, indeed, have joined in a stipulation with respect to the findings on deviation from the salinity requirement of the regulations. On the contrary, defendants insist that the time-temperature-salinity standards of the regulations cannot be met without rendering the product unmarketable. The defense, then, has taken the form of an all-out attack on the validity of the regulations involved.

"The attack centers on the unquestioned fact that only 21 U.S.C. §342(a)(4) can be looked to as the source of the Food and Drug Commissioner's authority to adopt the regulations. Defendants claim that it does not authorize any such regulation. . . . The contention takes a second form as an argument that in any event it would not suffice to show a violation of the regulation since the regulation is merely interpretive and not implementive of the law and, in consequence, the government must show that defendants violated the statute, reading the statute directly upon the facts; defendants say that no such showing of statutory violation has been made or attempted, for the Government has made no attempt to show any insanitary conditions at the plant if the word 'insanitary' is read in its ordinary sense, the sense invited by its use in the same context with the words 'contaminated' and 'filth.'

"It is next argued that the nature and professed object of the regulations was to minimize the hazard to the public of Type E botulism and the risks of foodborne infections in the consumption of smoked fish. It is argued that the regulations were put forward as the safest known processing parameters for preventing, through thermal destruction of spores of the bacteria, the outgrowth and toxin formation of *Clostridium botulinum* Type E. See Proposal of Part 128a for 21 CFR, 34 FR 17176 (October 16, 1969). It is argued that *C. botulinum* type Type E is not a contaminant that reaches the fish during processing but is undeniably taken up by the fish from the lake waters which are their natural habitat, and that the known material has long since made it perfectly clear that the risk visualized is remote and unreal in the case of smoked white fish. Defendants argue that to the extent this problem has been associated with smoked white fish, it has been associated with vacuum packaged white fish. That is a mode of packing not followed by the defendants and which apparently is no longer employed in the industry at all.

"The final phase of the attack rests on the argument that the regulation is unsupported by the record which it is entitled to call to its support. That record, it is argued, consists only of those materials submitted to the Commissioner by the industry and other interested parties in the course of the rule-making procedure and the materials brought forward and disclosed to the interested parties as being other materials consulted by the Commissioner in arriving at the regulations, to the extent that he did not rely solely on materials submitted in response to the notice of rule-making.

"1. There is no doubt that the Current Good Manufacturing Practice (sanitation) regulations, as they are frankly styled in 21 CFR §128(a)2, are adopted under 21 U.S.C. §342(a)(4), and that the Commissioner (as the delegate of the Secretary of Health, Education and Welfare, 21 CFR §2.120(a)(1), (15)) derived his rule-making authority in this relation solely from 21 U.S.C. §371(a) which provides simply that 'The authority to promulgate regulations for the efficient enforcement of this chapter, except as otherwise provided in this section, is vested in the Secretary.'

"Since the evidence is clear that the occurrence of *C. botulinum* Type E in white fish is not a fact or in the perspective of the statute a consequence of contaminations caused by unclean manufacturing practices or conditions, defendants' central argument is that the part of the Current Good Manufacturing Practice (sanitation) regulations here involved is, since oriented wholly to the sterilization of *C. botulinum* Type E occurring naturally in the fish and ingested in their native, water habitat, wholly unauthorized by the statute, and a nullity.

"As defendants point out, Section 342(a)(4) has not the specificity found in Section 344(a) dealing with the issuance, in emergencies, of temporary permits. These permits impose conditions governing the manufacturing process. They are issued when, in any locality, contamination with microorganisms is found to be occurring in the processing of any class of foods. And it could be said too that subdivision (4) does not use any of the general language used in other subdivisions of Section 342(a) which deal with substances in, the condition of, the source of, or the packaging of food: it does not use words like 'poisonous,' or 'deleterious,' or 'putrid,' or 'decomposed,' or 'diseased,' or 'unfit for food.' However it evinces a manifest and dominant purpose to deal with the cases in which the food has been prepared, packed or held under conditions whereby it *may have* become contaminated with filth or *may have* been rendered injurious to health. Describing the manufacturing condition as 'insanitary' is secondary: the word is given operative content only by reference to the purpose of subsection (a)(4), that is, to provide against whatever condition of processing may render the product injurious to health or contaminate it with filth.

"Only subdivision (4) of Section 342(a) treats a food as adulterated whether or not the food has in fact been contaminated or rendered injurious to health. Food is considered adulterated if it has been prepared, packed or held under conditions that *may have* resulted in its contamination or in its becoming injurious to health. It is the only one of the subdivisions which directly deals with processing rather than with product in defining the circumstances in which the food product will be considered adulterated. For purposes of subdivision (4), it is irrelevant that, by any other tests, the food could not have been determined to have been adulterated and could not have been condemned. While Section 342(a)(4) may literally seem to deal only with conditions brought about by processing itself, the regulation under review, Part 128a, is specifically addressed to setting processing parameters to prevent the 'outgrowth and toxin formation of *C. botulinum* Type E'. Seen in the perspective of Part 128a's purpose and the purpose of subsection (a)(4), the use of the word 'insanitary' in subdivision (4) of Section 342(a) is, at worst, inelegant, but it is not inadequate to include preparing, packing or holding conditions which permit a continuance of the outgrowth and toxin formation of the *C. botulinum* Type E in the product under process. Because such procedures may render the smoked fish injurious to health, the regulations proscribe cooking the fish at too low a temperature and/or for an insufficient length of time with inadequate salination. The approach of the regulations is that the temperature-time-salinity linkage is indispensable to preventing the outgrowth and toxin formation of the *C. botulinum* Type E. It is beside the point that the bacterial infestation here is not one that invades the fish during the processing. . . .

"Although the interpretation necessarily contended for by the Government puts a strain upon the language of the statute, it is a now familiar strain dictated by the manifest and dominant purpose of the statute—proscribing manufacturing processes that fail to deal effectively with a known risk of lethal infestation of food. The prescribed processing methods and controls are calculated to eliminate that risk.

"2. Defendants argue that Part 128a of 21 CFR is a merely interpretive regulation and is not coercive. The argument really is that Part 128a cannot be a substantive regulation having the effect of law. Defendants point out that the Act does not authorize any such substantive regulations under Section 342, although it does specifically authorize substantive regulations under those sections enumerated in 21 U.S.C. §371(e)(1). Those regulations are subjected, by Section 371(e), to strict promulgation requirements and broad opportunities for hearings. Section 371(e) also required that the determination be supported before the Secretary by detailed findings of fact based on substantial evidence of record, which are reviewable in the Court of Appeals rather than the District Court. The contention is that substantive effect may not, in this statutory setting, be ascribed to regulations adopted only under Section 371(a) and brought under judicial control only through 5 U.S.C. §501 *et seq* and §701 *et seq*.

"Whatever might have been the validity of the argument, it has been settled in this Circuit quite against defendants' contention by *National Nutritional Foods Association* v. *Weinberger*, 2d Cir. 1975, 512 F.2d 688, 694–698. Since the Food, Drug and Cosmetic Act does not require regulations not included under Section 371(e) to be made on the record after opportunity for an agency hearing, the rule making procedure invoked by the Commissioner in the present case is that of 5 U.S.C. §553 and the scope of review is correspondingly that of 5 U.S.C. §706(2), but without the requirement that the determination to adopt the regulation be supported by substantial evidence.

"There might have been debate as to how far the implications of the *Weinberger* v. *Hynson, Westcott and Gunning, Inc.*, 1973, 412 U.S. 609, 93 S.Ct. 2469, 37 L.Ed.2d 207, group of cases could be extrapolated. Those cases dealt with the new drugs application, approval and withdrawal-of-approval only provisions of 21 U.S.C. §355; those provisions are precisely drawn and deal with an intrinsically factual-adjudicative context in specific applications to definite pharmaceutical substances, and the possibly 'interpretive' regulations involved in the *Hynson* group of cases could be thought of as essentially procedural. But the resolution of the issue by Judge Mansfield in *National Nutritional Foods* is surely right, for the procedural regulations involved were what Mr. Justice Black once called 'outcome determinative' and not merely procedural regulations.

"So far as the form and language of Part 128a are concerned, they leave no room whatever for the argument that they were not intended to be 'substantive' and coercive if it was lawful for them to have that effect.

"3. Defendants argue that any possibility of injury to health from commercially prepared hot-smoked white fish was remote. Hence, defendants argue, there was no reasonable basis for concluding that the time-temperature-salinity prescriptions of Part 128a were necessary or appropriate to prevent the processing methods currently in use from rendering the fish injurious to health.

"It appears to be common knowledge in the industry that *C. botulinum* Type E is ubiquitous and that it occurs in the fresh water lakes from which white fish are drawn. Nearly all of the white fish of the industry in the greater metropolitan area come from Great Slave Lake and Winnipeg Lake; a small sample of white fish taken from Winnipeg Lake exhibited an 18 to 20% occurrence of *C. botulinum* Type E spores; a small sample from Great Slave Lake exhibited no spores. It appears also to be common knowledge in the industry that prior to 1963, cases of botulism that were traced to smoked white fish occurred but that there have been no occurrences since 1963. There appears also to be no controversy over the conclusion that vacuum packing of smoked fish, a practice no longer in use, was favorable to the spore development of toxin in smoked fish and was responsible for the 1960 and 1963 botulism outbreaks traced to white fish.

"At the hearing in this Court evidence was presented to the effect that the bacteria do not normally occur in the flesh of the fish but rather invade the skin and intestinal tract and migrate to the flesh, apparently in the course of evisceration and other preparation of the fish for brining, smoking and cooking. The same witness testified that since 1899 there had been ten outbreaks of botulism traced to *C. botulinum* Type E and that the toxin produced by the *C. botulinum* Type E spore development is a lethal toxin. It is common knowledge that botulism is an acute food poisoning marked by a high rate of mortality. . . .

"The Commissioner's proposal dated October 16, 1969, and published in the *Federal Register* on October 22, 1969 (34 FR 17—176) was prefaced by the statement that observations in smoked fish processing plants, made since 1963 by the FDA and other regulatory agencies, had shown that the industry had not consistently adhered to manufacturing processes that would minimize the hazard of Type E botulism and the risks of foodborne infections in the consumption of smoked fish. It recited further that the Bureau of Commercial Fisheries of the Department of the Interior had suggested that adequate time-temperature-salinity parameters had not yet been established for each individual species smoked other than chub, and that the Bureau had recommended that the proposed regulations be limited to plant sanitation and should exclude reference to processing techniques dealing with time-temperature relationships, or should describe good manufacturing techniques limited to smoked chub as processed in accordance with the food additive regulation governing the use of sodium nitrite (21 CFR §121.1230). . . .

"It is not denied or deniable that the *C. botulinum* Type E hazard is present and persistent, that the development of toxin occurs, and that it is controllable within acceptable limits by thermal destruction of spores and by maintenance of the fish and the smoked fish product under refrigeration except during the smoking and cooking phase. Nor is it denied or deniable that the Type E toxin is lethal and that botulism poisoning has a high rate of mortality.

"It may indeed be the fact that current product sampling of the cooked smoked white fish of defendants and of other producers in the greater metropolitan area did not disclose any evidence of botulinum spores, and that neither defendants nor others in the greater New York area have had any reported cases of botulism poisoning. That overlooks the fact that the regulations were imposed upon an industry already familiar with and using refrigeration and thermal destruction of spores. The cooking and smoking process itself and the brining of the white fish inevitably worked in the direction of Part 128a and its no doubt sterner requirements. The controversy is solely about what time-temperature-salinity parameters are appropriate to give assurance of safety to the consuming public and the fish processors; it is not about the propriety of establishing such parameters.

"It is not to be supposed that the 1960, 1963 occurrences of botulism in connection with hot-process smoked fish did not of itself cause changes in the industry. One of the communications to the Hearing Clerk in response to the notice of October 16, from the Association of Smoked Fish Processors, Inc., took exception to the FDA comment on industry practices. . . .

"Defendants by letter to the Hearing Clerk concurred in the Association's general submission but in addition made the point that certain of the proposed requirements were impossible or impractical, specifying that the heating of certain fish types to high temperatures would destroy the product completely and that very cold brining temperatures would not permit the absorption of salt by the fish. As an alternative to the time-temperature procedures, defendants suggested that specific processing procedures be established for each species after the completion of adequate work and experimentation. . . .

"In its submission to FDA, the Bureau of Commercial Fisheries of the Department of the Interior Fish and Wild Life Service (BCF) favored deferring specific controls until studies were completed with respect to the different species of smoked fish involved. . . . A detailed suggestion made by BCF was that the 180° 30 minute 3½% salt processing requirement be limited to smoked chub and should present the alternative of processing the chub with salt and nitrite at lower temperature in accordance with 21 CFR §121.1230.

"Similarly, neither the detailed response and commentary of the intervenor, National Fisheries Institute, Inc. nor its May 4, 1970 letter

. . . nor its letter of December 23, 1970 . . . in any way suggested that the *C. botulinum* Type E risk was not real enough to justify adopting a Part 128a in some significant form.

"4. The regulation as adopted is adequately supported by the record whether it is viewed as based on the Exhibit D tab A materials only or on all of Exhibit D. The regulation as modified from the original proposal is neither arbitrary nor capricious nor does it represent an abuse of discretion or any other deviation from law. The regulation was not adopted under a section enumerated under 21 U.S.C. §371(e) but rather under 21 U.S.C. §371(a). Therefore, it does not come within 5 U.S.C. §556 or §557 but rather within 5 U.S.C. §553(c), which simply requires that the agency, after considering the relevant matter presented, shall incorporate in the rules adopted a concise general statement of their basis and purpose.

"In adopting Part 128a under date of November 2, 1970 (published November 12, 1970, 35 FR 17,401) the Commissioner noted that the principal objection to the proposal had been that the process requirements in the proposed regulation could not be applied to all species of fish presently being smoked by the industry and that the regulations should therefore specify time-temperature requirements, as developed by research and study, on a species-by-species basis. The Commissioner then continued 'The Commissioner finds: (1) That although adequate times, temperatures and salt concentrations have not been demonstrated for each individual species of fish presently smoked, the processing requirements of the proposed regulations are the safest now known to prevent the outgrowth and toxin formation of *C. botulinum* Type E; and (2) that since the public health hazard of *C. botulinum* Type E in smoked fish is not restricted to a single species of fish, the conditions of current good manufacturing practice for this industry should be established without further delay.' . . .

"As noted above, Part 128a, as originally proposed, would have provided in Section 128a.7(d)(2) that all hot-process smoked fish, after brining to 3.5% salinity, should be heated to 180° F. for a minimum of 30 minutes with the exception of smoked chub containing sodium nitrite as provided for in Section 121.1230 (which had a lower temperature parameter). As adopted, Section 128a.7(d)(2) provided an alternative of either cooking for not less than 30 minutes at 180° F. if the fish was brined to contain 3.5% water phase salt or for 30 minutes at not less than 150° F. if the fish had been brined to contain 5% water phase salt. The alternative for sodium nitrite treated smoked chub was retained.

"The Association of Smoked Fish Processors, Inc., had argued that acceptable smoked chubs could not be prepared if the coldest portion of the slowest heating fish in the oven had to retain the temperature of 180° for 30 minutes and had argued that other varieties of fish were even more heat sensitive. The Association added 'Work now underway by the Bureau of Commercial Fisheries on several varieties of fish have indicated very encouraging preliminary results with lower temperature processing in combination with specific salt and nitrite levels.' The Bureau of Commercial Fisheries, as seen in the quotation above, had suggested an alternative of higher salt concentrations as an interim measure until species parameters could be evolved.

"The National Fisheries Institute, Inc., the intervenor, speaking for 26 firms actively smoking fish, had pointed out that smoked chub processed at 180° for 30 minutes had proved unacceptable to consumers, and that the matter had been resolved by permitting specified levels of sodium nitrite and chloride together with a lower operating temperature. It was said that if other fish were processed under similar high temperatures, the same marketing problems would arise. . . .

"The Commissioner's modification of Section 128a(d)(2) to incorporate the 150° 5% alternative met the industry's most clearly expressed objection. The regulation is certainly not expressl
form, as BCF may be thought to have suggested, but regu
not cut in stone. They are, inevitably, subject to continu
There is no indication that at any time before Part 128
mulgated, specific parameters for different varieties of fish
been developed and presented to the Commissioner as re
stitutes for the generalized requirement which is complain
present case. BCF did not present a petition to amend th
ditive (nitrite) regulation respecting smoked chub until
1971. They then proposed extending the regulation to wh
adjusting the processing parameters. The petition was incon
further studies were still in progress or in contemplation. T
(FDA No. 1A2671) was still under advisement at Januar
(Exhibit E)

"Other modifications in the proposal were made in resp
industry's suggestions. The suggestion of the owner of the
process (imparting smoky flavoring to fish) with respect
flavored fish resulted in the inclusion in Part 128a of pro
bracing smoke-flavored fish, which are treated with salt
smoke flavor by other than direct smoke action.

"The proposed regulation required entirely separate,
space for practically each distinct step in the processing of
fish, and commentators objected that this was impractical
not be accomplished in the industry's older plants. The
were acceded to—to the extent of providing that four
'should' be carried out in separate rooms or partitioned
of making the separate room or partitioned space require
datory only as to cooling and packing and storage of the fin
The provision governing inspection of raw fish was also
relaxed. The defrosting requirement was modified. The w
spraying provisions were altered. The testing provision w
Finally the provision covering the cooling of the smoke
cooking was materially relaxed.

"The Commissioner manifestly acted after considerin
ments submitted to him, and before final adoption, he
modified the proposal in accordance with the most impor
objections and suggestions submitted to him. No procee
ever instituted to review the regulations as adopted. Furth
later proceeding has been initiated formally and pressed
Commissioner directly to secure a modification of the regu
petition to the Commissioner (see Exhibit E) to extend
nitrite regulation to white fish and, perhaps, other fish ha
not yet been acted upon by the Commissioner. However, t
has not elected as it might have under 5 U.S.C. 704, 706 (
non-action in the nitrite matter as an unlawful withholdin
sonable delay of administrative action which should be c
a court. That does not mean that the FDA's failure to act
petition furnishes a ground for attacking its adoption of
the two matters are distinct in both time and substance. (T
oddly, overtones throughout the court hearing that the p
ceeding was an occasion to review the FDA's allegedly wr
action on the nitrite petition, and that the non-action som
lighted the action the FDA had taken in adopting Part 1

"On the formal administrative record, therefore, the a
Commissioner in adopting Part 128a was neither arbitrar
cious nor an abuse of discretion nor otherwise unauthori

"The regulations were authorized by the statute and th
ment denies no constitutional right to the parties defend

"5. The defendants argue in substance that, to an in
extent, those responsible for the determination to issue
the form in which it was finally issued had resort to some

material contained in defendants' exhibit D under tabs B through L. Apparently, it is not denied that the Commissioner had proper resort to the material under tab A, the more significant part of which has already been discussed, and which manifestly did effect modifications in the Commissioner's original proposal. Defendants argue that the Commissioner had no right, either directly or through his subordinate personnel, to resort to anything that was not accessible to and notified to those in interest, so that they could meet any material contained in the undisclosed matter that might influence the Commissioner. . . .

"A survey of the material under tabs B through L discloses nothing which undermines the provisions of Part 128a and it is not material of a kind that could lend itself to contradiction. The material consists almost entirely of neutral investigative studies apparently conducted with considerable scientific and practical sophistication. . . .

"The material comprised under Tabs B through L was made available to defendants and presumably to the intervenor during the discovery stages of the case. The expert and the industry evidence introduced at the trial is not at war with anything contained in the Tab B through Tab L material, and, in fact, added nothing of moment to what is in the formal record. Nothing in the B through L material has been or could well be pointed to as determining the Commissioner's conclusion, or as influencing it in such a way that, had it been known to be before him before the determination was made, it could have been met and refuted by other data. The problem did not and does not exist in that perspective or dimension. None of the B through L material suggests, nor do the defendants suggest, that precaution is unnecessary, that *C. botulinum* Type E is non-existent, that white fish come from untainted waters, or that there is any possibility that thermal treatment and salination and refrigeration can be dispensed with without danger to the industry or the public. If anything, the Commissioner's actions in modifying the original proposal demonstrate the openness of the proceeding. The very existence of the smoked-chub regulation (21 CFR §121.1230) authorizing the use of nitrite and a lower temperature demonstrates not only the industry's acquaintance with temperature-time-salinity parameters, but also shows the Commissioner's willingness to accede to scientific presentations.

"However, there is no ground for considering the material under Tabs B through L as being in the nature of *ex parte* evidence secretly acted upon to the disadvantage of the class affected by the adoption of Part 128a. In truth, the material contained under Tabs B through L comprises a reference library of the contemporary scientific work being done in the field, and to an extent, internal government views of the matter in the course of evolving a final administrative position. The internal evidence of the interdepartmental exchanges indicates that what the government was thinking about and doing was well known in the industry and to those who were actively interested in the inquiries being pursued as a result of the 1960 and 1963 poisonings, particularly the associations of interested persons. The rest of the material was published material which was either known to or readily accessible to any expert in the field to whom the members of the class to be affected by the regulation would naturally have turned for advice and assistance.

"The difference in viewpoint between the Bureau of Commercial Fisheries and the FDA, made perfectly plain in the October 1969 notice, was hardly a secret and was forthrightly dealt with by the FDA. The difference in viewpoint reflects the difference in the roles of the two departments of government, for the FDA had to be concerned not with the hot-process smoked fish processors but with the public safety and the sense of public security in the light of the 1960 and 1963 episodes.

"5. Defendants and the intervenor argue that the parameters established by the regulation are impossible of attainment in commercial operations. The evidence introduced at the trial tended to that showing, but it failed to make the showing. It demonstrated only that the processors who testified were unable to meet the parameters without material change in their processing practices. The cross-examination brought out numerous techniques that the industry had not yet exploited, including forced draft heat circulation in the oven, the use of humidifiers, and fresh approaches to the problems of obtaining uniformity of temperature throughout the ovens. . . .

"The evidence that a marketable product could not be prepared within the parameters suffers from essentially the same defect. The processors who testified were unable to produce marketable fish while staying within the regulation's parameters. But this was only shown to be true under their current processing practices. The taste test, although necessarily a narrow one, was carried out in as fair a manner as the trial situation permitted; if the results were accepted as a fair sampling of industry experience, they would lead to the conclusion that a product made under the parameters would not be marketable in the greater New York area nor probably in Florida. But that is hardly the issue. There are many other processors who may have mastered techniques that surmount the difficulties presented by the parameters. Moreover, the expectation cannot be that an identical product will be produced if the cooking temperature is materially increased and no compensating modifications, within the parameters, are introduced.

"The industry itself had faced the risk that if *C. botulinum* Type E was not dealt with effectively, its business would be destroyed. If the material under Tabs B through L shows anything, it shows that when Part 128a was proposed in late 1969 it was high time that some such proposal was made, no less in the industry's interest than in the public's interest in personal safety. It was for the industry to devise methods of preserving marketability within the parameters, if, as was inevitable, it was unable to bring forward adequate evidence that some other approach would serve the public interest.

"Finally, even if such a proposition could be demonstrated, it is not an answer to the regulation to say that marketable fish could not be processed under it. If that were the case it would simply mean that smoked white fish cannot be regarded as safe and that white fish cannot be processed in their only marketable form without an unacceptable threat to public health. The ultimate fact appears to be that the industry has not been able to come forward with alternative, safe processing means in which it has enough confidence to press them upon the Commissioner, and the industry has not exhausted the search for means of living within the parameters and still preparing marketable smoked white fish.

"It follows that the United States is entitled to an injunction requiring compliance with the challenged parameters. However, there is much to be said for the defendants' contentions with respect to the other items of non-compliance with the regulations which were turned up in the course of the inspections. These appear to be rather ordinary deviations from compliance which are readily and once-and-for-all curable by positive action. The evidence indicates that the defendants have taken positive corrective action as to those deviations and, on the basis of the present showing, the final decree need not and should not contain mandatory provisions in those respects. These operational deviations from the regulation do not have the shape of the resolute non-compliance with the time-temperature-salinity parameters which characterizes defendants' conduct of its processing plant up to the time of the second inspection.

"6. The defendants' trial evidence was taken over the Government's objection, reserving decision on the question of whether or not the

Government was on firm ground in its argument that the regulation was not subject to collateral attack through a *de novo* hearing. Expansion of the scope of the hearing to include evidence addressed to the validity and soundness of Part 128a served the two-fold purpose of being a species of *Citizens to Preserve Overton Park* v. *Volpe*, 401 U.S. 402, 91 S.Ct. 814, 28 L.Ed.2d 136 type hearing and of throwing light on the question of whether there was any occasion for an *Overton* type hearing to determine whether or not the Commissioner had acted rationally. If the case is, as the Government contends, controlled by testing Part 128a against the formal record, whether limited to the tab A material or extended to the tabs B to L material, the conclusion must be that Part 128a is fully supported and adequately supported in the formal record. Viewing the whole record, including all the trial evidence, it is concluded (for all the evidence, on review, is seen to exclude the need for any further *Overton* type hearing), that there is no necessity for any further hearing in this Court or for a remand to the Commissioner for reconsideration in the light of matters not before him or not adequately considered by him at the time the regulation was adopted. Of course that is not to say that if the nitrite research has now significantly progressed, the time may not be ripe for a petition to the Commissioner for modification of Part 128a along the lines of the smoked-chub regulation. As noted earlier, such a regulation as Part 128a survives under ambulatory review as the literature in the field opens up new possibilities of analysis of the botulism risk or new means of coping with the spore formation and toxin production of *C. botulinum* Type E.

"7. The Government will draft a decree in accordance with this opinion and either serve it on counsel for the defendants and for the intervenor with ten days notice of settlement, or, preferably, draft it in consultation with the defendants' and intervenor's counsel with a view to agreeing upon a form of decree—in the understanding that agreement on the form of the injunction does not to any extent imply acquiescence in its correctness as a disposition of the case."

In accordance with the opinion of the court, a decree of injunction was issued. The defendants appealed. Upon appeal, the court of appeals reversed the grant of the injunction and directed that the complaint be dismissed. In so ruling, the Court of Appeals said:

"This appeal involving a regulation of the Food and Drug Administration is not here upon a direct review of agency action. It is an appeal from a judgment of the District Court for the Eastern District of New York (Hon. John J. Dooling, Judge) enjoining the appellants, after a hearing, from processing hot smoked whitefish except in accordance with time-temperature-salinity (T-T-S) regulations contained in 21 CFR Part 122 (1977). The thorough analytical opinion of the District Court is reported at 417 F.Supp. 13674 (Aug. 17, 1976).

"The injunction was sought and granted on the ground that smoked whitefish which has been processed in violation of the T-T-S regulation is 'adulterated.' Food, Drug and Cosmetics Act ('the Act') §§302(a) and 301(k), 21 U.S.C. §§332(a), 331(k).

"Appellant Nova Scotia receives frozen or iced whitefish in interstate commerce which it processes by brining, smoking and cooking. The fish are then sold as smoked whitefish.

"The regulations cited above require that hot-process smoked fish be heated by a controlled heat process that provides a monitoring system positioned in as many strategic locations in the oven as necessary to assure a continuous temperature through each fish of not less than 180° F. for a minimum of 30 minutes for fish which have been brined to contain 3.5% water phase salt or at 150° F. for a minimum of 30 minutes if the salinity was at 5% water phase. Since *each* fish must meet these requirements, it is necessary to heat an entire batch of fish to even higher temperatures so that the lowest
temperature for any fish will meet the minimum requiremen

"Government inspection of appellants' plant established
question that the minimum T-T-S requirements were not be
There is no substantial claim that the plant was processing w
under 'insanitary conditions' in any other material respect.
lants, on their part, do not defend on the ground that they
compliance, but rather that the requirements could not be
marketable whitefish was to be produced. They defend upon the
that the regulation is invalid (1) because it is beyond the a
delegated by the statute; (2) because the FDA improperly reli
undisclosed evidence in promulgating the regulation and beca
not supported by the administrative record; and (3) because th
no adequate statement setting forth the basis of the regulat
reject the contention that the regulation is beyond the autho
egated by the statute, but we find serious inadequacies in
cedure followed in the promulgation of the regulation and h
be invalid as applied to the appellants herein. . . .

I

"The argument that the regulation is not supported by s
authority cannot be dismissed out of hand. . . . The sole s
authority relied upon is §342(a)(4), quoted above. As we
structed in *S. E. C.* v. *Chenery Corp.*, 318 U.S. 80, 87, 63 S.
459, 87 L.Ed. 626 (1943) (Chenery I), '[t]he grounds upon w
administrative order must be judged are those upon which th
discloses that its action was based.' Nor is the Commissior
pressed reliance solely on §342(a)(4) a technicality which m
removed by a later and wiser reliance on another subsection
this case, as the agency recognized, there is no other section
section that can pass as statutory authority for the regulati
categories of 'adulteration' prohibited in Section 342 all refer
as an 'adulterated' *product* rather than to the *process* of p
food, except for subsection (a)(4) which alone deals with th
essing of food.

"Appellants contend that the prohibition against 'insanita
ditions' embraces conditions only in the plant itself, but d
include conditions which merely inhibit the growth of organ
ready in the food when it enters the plant in its raw stat
distinguish between conditions which are insanitary, which th
cede to be within the ambit of §342(a)(4), and conditions o
zation required to destroy micro-organisms, which they cont
not.

"It is true that on a first reading the language of the su
appears to cover only 'insanitary conditions' '*whereby* it [th
may have been rendered injurious to health' (emphasis adde
a plausible argument can, indeed, be made that the reference
insanitary conditions in the plant itself, such as the presence of
or insects. . . .

"Yet, when we are dealing with the public health, the lang
the Food, Drug and Cosmetic Act should not be read too restr
but rather as 'consistent with the Act's overriding purpose to
the public health.' . . .

"Section 371(a), applicable to rulemaking under §342(a)(
vides: 'The authority to promulgate regulations for the effic
forcement of this chapter, except as otherwise provided in this
is vested in the Secretary.' We read this grant as analogou
provision 'make . . . such rules and regulations as may be n
to carry out the provisions of this Act,' in which case 'the va
a regulation promulgated thereunder will be sustained so lon
'reasonably related to the purposes of the enabling legislati
tations omitted] *Mourning* v. *Family Publications Service, I*
U.S. 356, 369, 93 S.Ct. 1652, 36 L.Ed.2d 318 (1973). Wher

rulemaking serves the purposes of the statute, courts should refuse to adopt a narrow construction of the enabling legislation which would undercut the agency's authority to promulgate such rules. . . . The court's role should be one of constructive cooperation with the agency in furtherance of the public interest. . . .

"Appellant's argument, it should be noted, is not that there has been an unlawful delegation of legislative power. . . . even a delegation of 'unfettered discretion.' . . . The argument, fairly construed, is that Congress did not mean to go so far as to require sterilization sufficient to kill bacteria that may be in the food itself rather than bacteria which accreted in the factory through the use of insanitary equipment.

"There are arguments which can indeed be mustered to support such a broad-based attack under 5 U.S.C. §706. . . .

"We do not discount the logical arguments in support of a restrictive reading of §342(a)(4), but we perceive a larger general purpose on the part of Congress in protecting the public health.

"We come to this conclusion, aside from the general rules of construction noted above, for several reasons: First, until this enforcement proceeding was begun, no lawyer at the knowledgeable Food and Drug bar ever raised the question of lack of statutory delegation or even hinted at such a question. Second, the body of data gathered by the experts, including those of the Technical Laboratory of the Bureau of Fisheries manifested a concern about the hazards of botulism. Third, analogously, the Meat Inspection Act of 1907 (now codified as amended at 21 U.S.C. §608), which hardly provided a clearer standard than does the 'insanitary conditions' provision in the Food and Drug Act, has regulations under it concerning mandatory temperatures for processing pork muscle tissue to eliminate the hazard of trichinosis. . . . These regulations have been assumed for years to have been properly promulgated by the Secretary of Agriculture under the statutory authority given to him.

"Lastly, a holding that the regulation of smoked fish against the hazards of botulism is invalid for lack of authority would probably invalidate, to the extent that our ruling would be followed, the regulations concerning the purity of raw materials before their entry into the manufacturing process in 21 CFR Part 113 (1977) (inspection of incoming raw materials for microbiological contamination before thermal processing of low-acid foods packed in hermetically sealed containers), in 21 CFR Part 118 (1977) (pasteurization of milk and egg products to destroy Salmonella micro-organisms before use of the products in cacao products and confectionery), and 21 CFR Part 129 (1977) (product water supply for processing and bottling of bottled drinking water must be of a safe, sanitary quality when it enters the process).

"The public interest will not permit invalidation simply on the basis of a lack of delegated statutory authority in this case. A gap in public health protection should not be created in the absence of a compelling reading based upon the utter absence of any statutory authority, even read expansively. Here we find no congressional history on the specific issue involved, and hence no impediment to the broader reading based on general purpose. We believe, nevertheless, that it would be in the public interest for Congress to consider in the light of existing knowledge, a legislative scheme for administrative regulation of the processing of food where hazard from micro-organisms in food in its natural state may require affirmative procedures of sterilization. This would entail, as well, a decision on the type of rulemaking procedure Congress thinks fit to impose.

II

"Appellants contend that there is an inadequate administrative record upon which to predicate judicial review, and that the failure to disclose to interested persons the factual material upon which the agency was relying vitiates the element of fairness which is essential to any kind of administrative action. Moreover, they argue that the 'concise general statement of . . . basis and purpose' by the Commissioner was inadequate. 5 U.S.C. § 553.

"The question of what is an adequate 'record' in informal rulemaking has engaged the attention of commentators for several years. The extent of the administrative record required for judicial review of informal rulemaking is largely a function of the scope of judicial review. Even when the standard of review is whether the promulgation of the rule was 'arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law,' as specified in 5 U.S.C. §706(2)(A), judicial review must nevertheless, be based on the 'whole record' (*id.*). Adequate review of a determination requires an adequate record, if the review is to be meaningful. . . .

"This raises several questions regarding the informal rulemaking procedure followed here: (1) What record does a reviewing court look to? (2) How much of what the agency relied on should have been disclosed to interested persons? (3) To what extent must the agency respond to criticism that is material?

A

"With respect to the content of the administrative 'record,' the Supreme Court has told us that in informal rulemaking, 'the focal point for judicial review should be the administrative record already in existence, not some new record made initially in the reviewing court.'. .

"No contemporaneous record was made or certified. When, during the enforcement action, the basis for the regulation was sought through pretrial discovery, the record was created by searching the files of the FDA and the memories of those who participated in the process of rulemaking. This resulted in what became Exhibit D at the trial of the injunction action. Exhibit D consists of (1) Tab A containing the comments received from outside parties during the administrative 'notice-and-comment' proceeding and (2) Tabs B through L consisting of scientific data and the like upon which the Commissioner now says he relied but which were not made known to the interested parties.

"Appellants object to the exclusion of evidence in the District Court 'aimed directly at showing that the scientific evidence relied upon by the FDA was inaccurate and not based upon a realistic appraisal of the true facts. Appellants attempted to introduce scientific evidence to demonstrate that in fixing the processing parameters FDA relied upon tests in which ground fish were injected with many millions of botulism [sic] spores and then tested for outgrowth at various processing levels whereas the spore levels in nature are far less and outgrowth would have been prevented by far less stringent processing parameters.' (Br. p. 33). The District Court properly excluded the evidence.

"In an enforcement action, we must rely exclusively on the record made before the agency to determine the validity of the regulation. The exception to the exclusivity of that record is that 'there may be independent judicial fact-finding when issues that were not before the agency are raised in a proceeding to *enforce* non-adjudicatory agency action.' *Overton Park, supra,* 401 U.S. at 415, 91 S.Ct. at 823 (1971). (Emphasis added.)

"Though this is an enforcement proceeding and the question is close, we think that the 'issues' were fairly before the agency and hence that *de novo* evidence was properly excluded by Judge Dooling. *Camp* v. *Pitts, supra.* Our concern is, rather, with the manner in which the agency treated the issues tendered.

B

"The key issues were (1) whether, in the light of the rather scant history of botulism in whitefish, that species should have been considered separately rather than included in a general regulation which failed to distinguish species from species; (2) whether the application of the proposed T-T-S requirements to smoked whitefish made the whitefish commercially unsaleable; and (3) whether the agency recognized that prospect, but nevertheless decided that the public health needs should prevail even if that meant commercial death for the whitefish industry. The procedural issues were: whether, in the light of these key questions, the agency procedure was inadequate because (i) it failed to disclose to interested parties the scientific data and the methodology upon which it relied; and (ii) because it failed utterly to address itself to the pertinent question of commercial feasibility.

1.

The History of Botulism in Whitefish

"The history of botulism occurrence in whitefish, as established in the trial record, which we must assume was available to the FDA in 1970, is as follows. Between 1899 and 1964 there were only eight cases of botulism reported as attributable to hot-smoked whitefish. In all eight instances, vacuum-packed whitefish was involved. All of the eight cases occurred in 1960 and 1963. The industry has abandoned vacuum-packing, and there has not been a single case of botulism associated with commercially prepared whitefish since 1963, though 2,750,000 pounds of whitefish are processed annually. Thus, in the seven-year period from 1964 through 1970, 17.25 million pounds of whitefish have been commercially processed in the United States without a single reported case of botulism. The evidence also disclosed that defendant Nova Scotia has been in business some 56 years, and that there has never been a case of botulism illness from the whitefish processed by it.

2.

The Scientific Data

"Interested parties were not informed of the scientific data, or at least of a selection of such data deemed important by the agency, so that comments could be addressed to the data. Appellants argue that unless the scientific data relied upon by the agency are spread upon the public records, criticism of the methodology used or the meaning to be inferred from the data is rendered impossible.

"We agree with appellants in this case, for although we recognize that an agency may resort to its own expertise outside the record in an informal rulemaking procedure, we do not believe that when the pertinent research material is readily available and the agency has no special expertise on the precise parameters involved, there is any reason to conceal the scientific data relied upon from the interested parties. . . .

"Here all the scientific research was collected by the agency, and none of it was disclosed to interested parties as the material upon which the proposed rule would be fashioned. Nor was an articulate effort made to connect the scientific requirements to available technology that would make commercial survival possible, though the burden of proof was on the agency. This required it to 'bear a burden of adducing a reasoned presentation supporting the reliability of its methodology.' . . .

"Though a reviewing court will not match submission against countersubmission to decide whether the agency was correct in its conclusion on scientific matters (unless that conclusion is arbitrary), it will consider whether the agency has taken account of all 'relevant factors and whether there has been a clear error of judgment.' . . . In this circuit we have said that 'it is "arbitrary or capricious" for an agency not to take into account all relevant factors in making its determination.' . . .

"If the failure to notify interested persons of the scientific research upon which the agency was relying actually prevented the presentation of relevant comment, the agency may be held not to have considered all 'the relevant factors.' We can think of no sound reasons for secrecy or reluctance to expose to public view (with an exception for trade secrets or national security) the ingredients of the deliberative process. . . . Indeed, the FDA's own regulations now specifically require that every notice of proposed rulemaking contain 'references to all data and information on which the Commissioner relies for the proposal (copies or a full list of which shall be a part of the administrative file on the matter . . .).' 21 CFR §10.40(b)(1) (1977). And this is, undoubtedly, the trend. . . .

"We think that the scientific data should have been disclosed to focus on the proper interpretation of 'insanitary conditions.' When the basis for a proposed rule is a scientific decision, the scientific material which is believed to support the rule should be exposed to the view of interested parties for their comment. One cannot ask for comment on a scientific paper without allowing the participants to read the paper. Scientific research is sometimes rejected for diverse inadequacies of methodology; and statistical results are sometimes rebutted because of a lack of adequate gathering technique or of supportable extrapolation. Such is the stuff of scientific debate. To suppress meaningful comment by failure to disclose the basic data relied upon is akin to rejecting comment altogether. For unless there is common ground, the comments are unlikely to be of a quality that might impress a careful agency. The inadequacy of comment in turn leads in the direction of arbitrary decision-making. We do not speak of findings of fact, for such are not technically required in the informal rulemaking procedures. We speak rather of what the agency should make known so as to elicit comments that probe the fundamentals. Informal rulemaking does not lend itself to a rigid pattern. Especially, in the circumstance of our broad reading of statutory authority in support of the agency, we conclude that the failure to disclose to interested persons the scientific data upon which the FDA relied was procedurally erroneous. Moreover, the burden was upon the agency to articulate rationally why the rule should apply to a large and diverse class, with the same T-T-S parameters made applicable to *all* species. . . .

C

"Appellants additionally attack the 'concise general statement' required by APA, 5 U.S.C. §553, as inadequate. We think that, in the circumstances, it was less than adequate. It is not in keeping with the rational process to leave vital questions, raised by comments which are of cogent materiality, completely unanswered. The agencies certainly have a good deal of discretion in expressing the basis of a rule, but the agencies do not have quite the prerogative of obscurantism reserved to legislatures. . . .

"The test of adequacy of the 'concise general statement' was expressed by Judge McGowan in the following terms: 'We do not expect the agency to discuss every item of fact or opinion included in the submissions made to it in informal rulemaking. We do expect that, if the judicial review which Congress has thought it important to provide is to be meaningful, the "concise general statement of . . . basis and purpose" mandated by Section 4 will enable us to see what major issues of policy were ventilated by the informal proceedings and why the agency reacted to them as it did.' . . .

"And Judge Friendly has noted that '[i]n a case where a proposed standard under OSHA [Occupational Safety and Health Act] has been opposed on grounds as substantial as those presented here, the Department has the burden of offering *some* reasoned explanation.' . . . (emphasis in original).

"The Secretary was squarely faced with the question whether it was necessary to formulate a rule with specific parameters that applied to all species of fish, and particularly whether lower temperatures with the addition of nitrite and salt would not be sufficient. Though this alternative was suggested by an agency of the federal government, its suggestion, though acknowledged, was never answered.

"Moreover, the comment that to apply the proposed T-T-S requirements to whitefish would destroy the commercial product was neither discussed nor answered. We think that to sanction silence in the face of such vital questions would be to make the statutory requirement of a 'concise general statement' less than an adequate safeguard against arbitrary decision-making. . . .

"One may recognize that even commercial infeasibility cannot stand in the way of an overwhelming public interest. Yet the administrative process should disclose, at least, whether the proposed regulation is considered to be commercially feasible, or whether other considerations prevail even if commercial infeasibility is acknowledged. This kind of forthright disclosure and basic statement was lacking in the formulation of the T-T-S standard made applicable to whitefish. It is easy enough for an administrator to ban everything. In the regulation of food processing, the worldwide need for food also must be taken into account in formulating measures taken for the protection of health. In the light of the history of smoked whitefish to which we have referred, we find no articulate balancing here sufficient to make the procedure followed less than arbitrary.

"After seven years of relative inaction, the FDA has apparently not reviewed the T-T-S regulations in the light of present scientific knowledge and experience. In the absence of a new statutory directive by Congress regarding control of micro-organisms, which we hope will be worthy of its consideration, we think that the T-T-S standards should be reviewed again by the FDA.

"We cannot, on this appeal, remand to the agency to allow further comments by interested parties, addressed to the scientific data now disclosed at the trial below. We hold in this enforcement proceeding, therefore, that the regulation, as it affects nonvacuum-packed hot-smoked whitefish, was promulgated in an arbitrary manner and is invalid.

"When the District Court held the regulation to be valid, it properly exercised its discretion to grant the injunction. In view of our conclusion to the contrary, we must reverse the grant of the injunction and direct that the complaint be dismissed." (Inj. No. 728; S. No. 76-41-506 et al.; N.J. No. 45)

Vollmers Bakery, Inc., and **Paul A. Petry,** president, Denver, Dist. Colo. Charged 12-30-77 in a complaint for injunction: that the defendants had been engaged at their Denver bakeries in holding for sale after interstate shipment various bakery ingredients such as flour, crushed wheat and milk replacer, and engaged in preparing, packing, holding and distributing in interstate commerce bakery products such as bread, rolls, buns and sweet bakery products which contained interstate components; that the crushed wheat and milk replacer contained insect filth and the flour, crushed wheat, milk replacer in other bakery products had been prepared, packed and held under insanitary conditions; that FDA inspections disclosed a number of specified insanitary conditions and practices; and that the defendants had been warned of insanitary conditions and practices in their bakeries on a number of occasions; 402(a)(3) and (4).

The defendants moved to suppress all pleading, papers and proceedings in the action until the court found merit in the charges or found good cause to open the file to the public. The court granted the motion. Upon the government's motion for reconsiderations, the court modified its order as follows:

"That the Food and Drug Administration shall in no way be restrained from complying with any of its regulations or internal policies and practices requiring the publication or release of any internal reports, judgments, decrees, or court orders rendered in connection with the final adjudication of this matter:

"That the Food and Drug Administration shall in no way be restrained from furnishing any information or documents contained in FDA files which is authorized or required by law to be furnished pursuant to requests made under the Freedom of Information Act."

A consent decree of permanent injunction enjoined the complained of violations. Subsequently FDA inspection revealed that the defendant's establishment appeared to be in compliance with the specified terms of the decree; and the establishment was classified as an "approved" supplier for interstate carriers. (Inj. No. 821; S. No. 78-117-331 et al.; N.J. No. 46)

NOTICE OF JUDGMENT on Miscellaneous Actions

Supplemental New Animal Drug Applications for furazolidone, and **FDA's refusal to approve additional bulk supplier sources,** Washington, Dist. Petitioned 7-14-77 by Rhodia, Inc., Hess & Clark Div., Ashland, Ohio, against FDA in a suit for judicial review: that the court set aside the FDA order of May 20, 1977, refusing to approve supplemental new animal drug applications proposing changes in NADA's 9-073, 11-698 and 12-061, to provide for alternate suppliers of the bulk drug substance used for manufacture of furazolidone products under those New Animal Drug Applications.

The Court of Appeals set aside the FDA's order, saying:

"Rhodia, Inc., Hess & Clark Division (Rhodia) sought to amend approved new animal drug applications (NADA's) in effect for three products containing the active drug furazolidone so as to include new sources of supply of the bulk drug in addition to the one named in the original NADA's. The Director of the Bureau of Veterinary Medicine of the Food and Drug Administration (FDA) denied approval of Rhodia's supplemental NADA's. Finding the action arbitrary and capricious, we set aside the FDA order and remand for further proceedings.

I. *Background*

"Rhodia currently holds three approved NADA's for products used in the treatment of infectious and parasitic conditions in poultry and swine that contain the active ingredient furazolidone. At the time of Rhodia's initial applications in the 1950's, the Norwich Pharmacal Company held the patent on furazolidone and was listed by Rhodia in its applications as the sole source of supply of the bulk drug.

"Evidence casting doubt on the safety of furazolidone prompted FDA to propose the withdrawal of approval of the drug for use in food-producing animals. On August 4, 1971, the agency published a notice of opportunity for hearing on the proposed withdrawal, alleging that furazolidone had been shown to cause tumors in laboratory animals, and that, in the absence of 'appropriately sensitive' methods of establishing the absence of furazolidone residues from food produced by treated animals, the drug was no longer shown to be safe. 36 Fed.Reg. 14,342 (1971). Rhodia requested a hearing, but none was held, and no action was taken on that proposal to withdraw approval.

"On May 13, 1976, the FDA withdrew its original notice of opportunity and issued a new notice. The new notice cited evidence that furazolidone induced cancer in laboratory animals and concluded that, in the absence of adequate, reliable and practicable methods of analysis to detect the drug's presence in food derived from treated animals, approval of the drug must be withdrawn. 41 Fed.Reg. 19,906, 19,907 (1976). Again, Rhodia requested a hearing; though FDA issued a notice of intent to hold a hearing, 42 Fed.Reg. 18,660 (1977), that hearing has yet to be held.

"Rhodia first sought to supplement its NADA's to add an alternative supplier of bulk furazolidone in December, 1972. The change was necessary because Norwich had terminated its supply agreement with Rhodia. The Director of the Division of New Animal Drugs of the Bureau of Veterinary Medicine refused to approve the supplemental NADA's. While acknowledging that the bulk drug to be supplied by the alternate supplier would meet the quality specifications for furazolidone, the Director stated that Rhodia's applications would remain incomplete 'pending FDA's acceptance and validation of the more sensitive methods of analysis to establish the absence of the drug in food derived from treated animals.' . . .

"In reaching this decision, the Director evidently applied an FDA policy that approval of a supplemental NADA constituted an affirmation that all safety and effectiveness information contained in the NADA as a whole was scientifically accurate by current standards. Thus, submission of a supplemental NADA triggered a review by the FDA of all the safety and effectiveness data underlying the original application. As a result, approval of a supplemental NADA was precluded in situations like that of furazolidone, until questions of the safety of the drug were resolved. *See* 41 Fed. Reg. 50,003 (1976).

"However, FDA policy in practice accepted some supplements, even though the validity of a NADA was under review, at least where safety would be enhanced by a supplement. Apparently Rhodia was of the belief that the FDA would acquiesce in its change of suppliers, and put that change into effect. On March 8, 1977, however, the Cincinnati district office of the FDA informed Rhodia that continued marketing of products containing furazolidone not supplied by Norwich (the supplier named in the approved NADA's) was unlawful. Rhodia ceased marketing products containing furazolidone supplied by alternate suppliers and negotiated an agreement with Norwich to resume supplying it bulk furazolidone.

"On March 11, 1977, Rhodia again submitted supplemental NADA's naming alternate suppliers of bulk furazolidone. The Acting Chief of the Division of Drugs for Avian Species in the Bureau of Veterinary Medicine refused to approve the supplements. On May 20, 1977, following protest by Rhodia, the Director of the Bureau affirmed.

"The Director invoked a revised FDA policy on supplemental NADA's, adopted by the Agency on November 12, 1976. 41 Fed.Reg. 50,003 (1976). Under that revised policy, approval of a supplemental NADA was permitted without a full safety and effectiveness review if approval of the supplement would not 'entail any increase in potential risk of human exposure to drug residues.' Pointing to the pending proceedings to withdraw approval of furazolidone as carcinogenic, the Director noted that the FDA had to be 'especially alert' to increases in potential risk until the safety questions were resolved. In essence, the Director found that to add new approved sources of supply would likely increase the aggregate quantity of furazolidone marketed and consumed, with resultant increase in the potential risk of human exposure to its residues. . . . Rhodia asks this court to set aside the order as 'plainly unlawful.'

II. *Analysis*

"We find it unnecessary to decide whether the FDA is within the law in adopting a policy that requires a full safety and effectiveness review before a supplemental NADA may be approved. Assuming that it has such authority, we find the FDA's application of its policy to deny approval of Rhodia's supplemental NADA's to be arbitrary and capricious.

"The Director of the Bureau of Veterinary Medicine concluded that Rhodia's proposed changes to add approved suppliers of bulk furazolidone would entail an 'increase in potential risk of human exposure to drug residues.' The theory was not that the changes would affect the quality of the new animal drug in such a way as to call into question the drug's safety, but rather that safety was threatened because the addition of suppliers might result in an increase in the quantity of furazolidone on the market.

"There is no indication that the FDA has previously considered changes in a NADA that will increase available quantities of a new animal drug to bear on the safety of the drug. Indeed, the contrary appears to be the case. The FDA's own regulations affirmatively exclude from the approval requirement certain NADA changes that appear to possess a potential for increasing quantities on the market similar to, or even greater than, that of changes in approved suppliers. Changes in equipment, including the enlargement of plant capacity that do not alter the method of manufacture, and changes in commercial batch size, are permitted without the submission or approval of a supplemental NADA. 21 CFR § 514.8(a)(5)(iii), (iv) (1978). An applicant may add new distributors of an approved drug automatically upon submission of a supplemental NADA for which no approval is required. *Id.*, §514.8(a)(6). Further, there is no check on the ability of a supplier of an applicant's bulk drug to increase its manufacturing capacity (and thus the quantity of drug available to the applicant).

"Furthermore, Rhodia asserts that the FDA's regulations do not require that bulk suppliers be named in the NADA at all, but only that the NADA state that materials of specified quality or purity will be used. If so, the FDA's control over Rhodia's supplemental NADA's would stem from a fortuity that Norwich was named as supplier in the original NADA's, a circumstance probably ascribable to the fact that Norwich was at the time the sole supplier of bulk furazolidone. The FDA disputes Rhodia's construction of the applicable regulations. We do not parse the regulations to determine which position is correct, for the FDA does not refute Rhodia's assertion that it has in practice approved NADA's that do not specify a particular bulk drug supplier, but merely state that the ingredients obtained, from whatever source, will meet prescribed standards.

"The FDA has the authority, and it has the responsibility, to define those changes that bear on safety so as to invoke the full safety and effectiveness review required by its supplemental NADA policy. Thus far, the FDA has not structured its regulations to define quantity as a factor triggering invocation of the safety review. Once it channels its discretion in a certain manner (here by excluding from the approval requirement certain types of NADA's, and by a practice of approving original NADA's that do not name a specific supplier), the agency should follow that course consistently or articulate reasons for departure. In view of its previous course, bypassing quantity as a determinative criterion, the FDA may not now latch onto this factor as the basis for rejecting an otherwise-unobjectionable supplemental NADA because of pre-existing doubts as to the safety of the product. The FDA did not offer, nor can we discern from the record, any rational basis for distinguishing the proposed change of suppliers here from other changes that would result in increased quantities on the market or from the FDA's earlier approval of supplemental NADA's not naming a specific supplier. Therefore we vacate the FDA order denying the supplemental application." (Misc. No. 442; N.J. No. 47)

Notices of Judgment are given pursuant to section 705 of the Federal Food, Drug, and Cosmetic Act. Notices of Judgment report cases involving seizure proceedings, criminal proceedings, and injunction proceedings. Seizure proceedings are civil actions taken against *goods* alleged to be in violation, and criminal and injunction proceedings are against *firms* or *individuals* charged to be responsible for violations. The cases generally involve foods, drugs, devices, or cosmetics which were alleged to be adulterated or misbranded or otherwise violative of the law when introduced into and while in interstate commerce, or while held for sale after shipment in interstate commerce.

Notices of Judgment are prepared by Food and Drug Division, Office of the General Counsel, HHS.

Published by direction of the Secretary of Health and Human Services.

Arthur Hull Hayes Jr., M.D., *Commissioner of Food and Drugs*
Washington, D.C., Feb. 1, 1982

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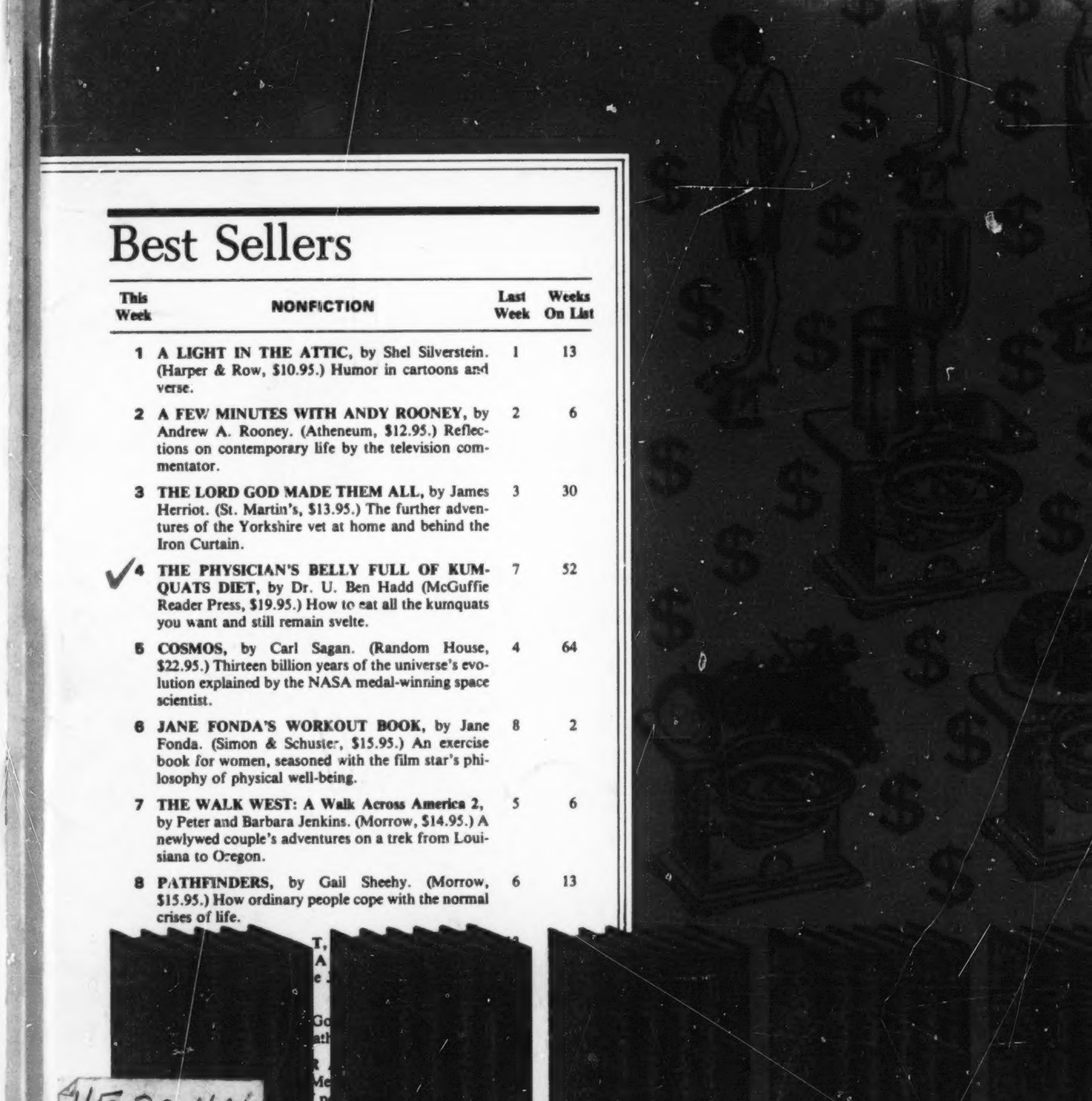
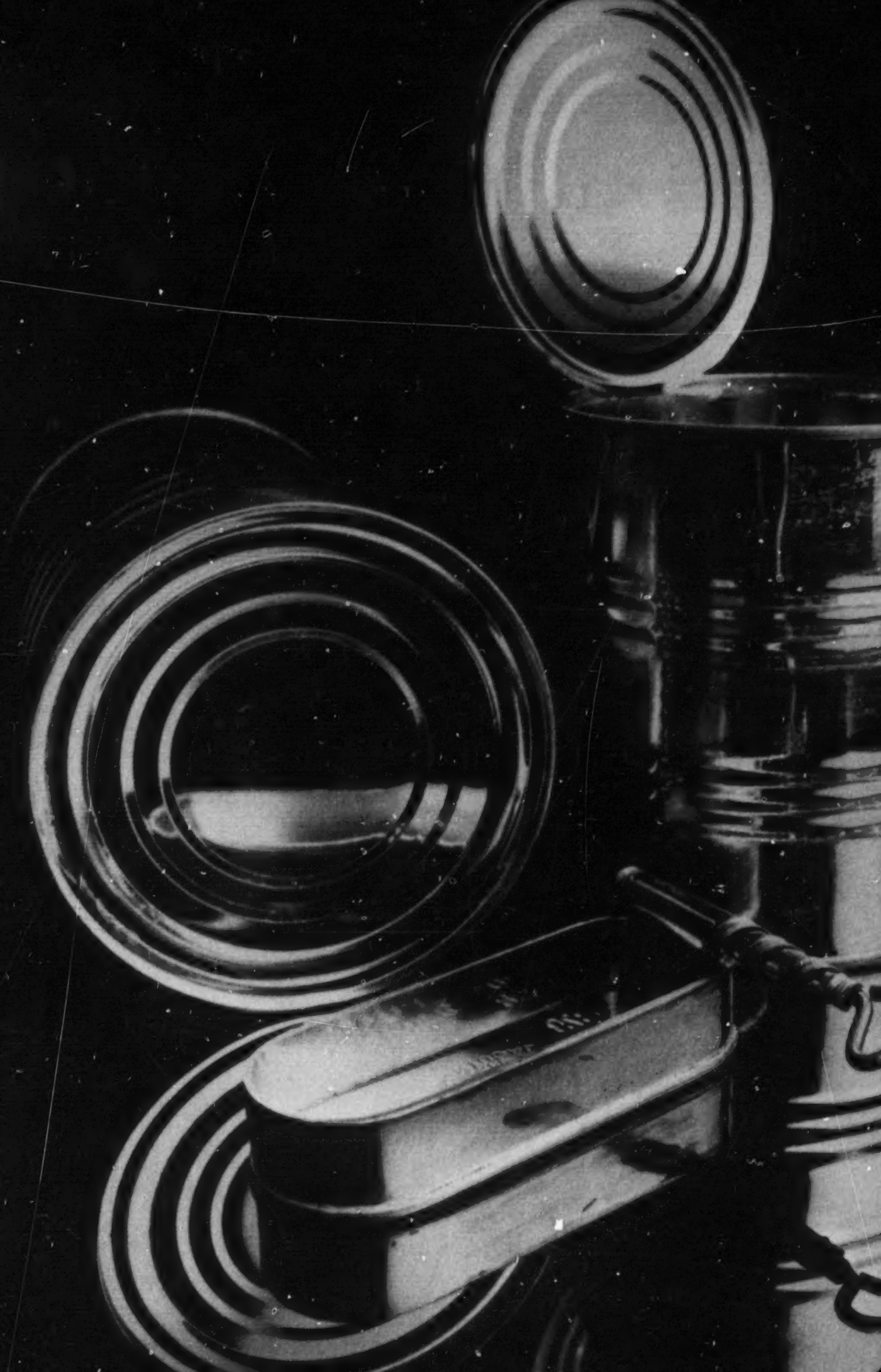


Best Sellers

This Week	NONFICTION	Last Week	Weeks On List
1	**A LIGHT IN THE ATTIC,** by Shel Silverstein. (Harper & Row, $10.95.) Humor in cartoons and verse.	1	13
2	**A FEW MINUTES WITH ANDY ROONEY,** by Andrew A. Rooney. (Atheneum, $12.95.) Reflections on contemporary life by the television commentator.	2	6
3	**THE LORD GOD MADE THEM ALL,** by James Herriot. (St. Martin's, $13.95.) The further adventures of the Yorkshire vet at home and behind the Iron Curtain.	3	30
✓4	**THE PHYSICIAN'S BELLY FULL OF KUMQUATS DIET,** by Dr. U. Ben Hadd (McGuffie Reader Press, $19.95.) How to eat all the kumquats you want and still remain svelte.	7	52
5	**COSMOS,** by Carl Sagan. (Random House, $22.95.) Thirteen billion years of the universe's evolution explained by the NASA medal-winning space scientist.	4	64
6	**JANE FONDA'S WORKOUT BOOK,** by Jane Fonda. (Simon & Schuster, $15.95.) An exercise book for women, seasoned with the film star's philosophy of physical well-being.	8	2
7	**THE WALK WEST: A Walk Across America 2,** by Peter and Barbara Jenkins. (Morrow, $14.95.) A newlywed couple's adventures on a trek from Louisiana to Oregon.	5	6
8	**PATHFINDERS,** by Gail Sheehy. (Morrow, $15.95.) How ordinary people cope with the normal crises of life.	6	13



FDA CONSUMER

VOL. 16 NO. 2

New Routes for Drugs To Travel
Today drugs might be pasted on the skin in a form of adhesi bandage. No longer is the medical profession limited to prescribing medicines that are taken orally or injected.

Cookware as a Source of Additives
Food can be adulterated by the pot or pan it is cooked in Here's a look at aluminum, copper and ceramic utensils.

Diet Books Sell Well But . . .
It seems there is always a place near the top of the best se ler list for a diet book. But, as this article points out, few of th diets offered are sensible ones and some are even dangerou

On Getting the Lead Out of Food
Lead is a poison and some of it gets into our systems fro canned food. This article tells what FDA and the canning i dustry are doing to cut down on the amount of lead we ingest that manner.

Some OTC Drugs That Work, Some That Don't
More reports to FDA from panels of outside experts on ove the-counter medicines. These cover smoking inhibitors, ora insect repellents, bellyache remedies, corn and callus treatments, hormone products and mercury compounds.

Pregnant Women Heed Advice
A recent nationwide survey showed that women are aware possible health dangers that may arise from caffeine and alcohol consumed during pregnancy.

Updates

The Notebook

Investigators' Reports

Seizures and Postal Service Cases

Notices of Judgment

Some 20 billion cans a year, like those pictured at left, are food in this country. Most of them are sealed with lead sold poisonous. And therein lies a problem, discussed in On Gett Out of Food *on page 18.*

MARCH 1982

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Richard S. Schweiker
Secretary, U.S. Department of Health and Human Services

Arthur Hull Hayes Jr., M.D.
Commissioner of Food and Drugs

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Section 705 [375] of the Food, Drug, and Cosmetic Act:
(a) The Secretary shall cause to be published from time to time reports summarizing all judgments, decrees, and court orders which have been rendered under this Act, including the nature of charge and the disposition thereof.
(b) The Secretary may also cause to be disseminated information regarding food, drugs, devices, or cosmetics in situations involving, in the opinion of the Secretary, imminent danger to health, or gross deception of the consumer. Nothing in this section shall be construed to prohibit the Secretary from collecting, reporting, and illustrating the results of the investigations of the Department.

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million new victims — enough to populate a large city. Yet we only have enough
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Updates

Another Look at Fats

Fats in the diet are important sources of nutrients and are responsible for many of the characteristic flavors, aromas and textures found in food, according to a Scientific Status Summary released in December 1981 by the Institute of Food Technologists. Fats also are the most concentrated sources of food energy in the diet yielding nine calories per gram, over twice as many calories as are supplied by either carbohydrates or protein. However, the report also concluded that some people may need to limit their intake of fats.

Fat consumption in North America has increased significantly during this century, the report of the Chicago-based institute points out. This increased consumption includes both visible and invisible fats as well as fats and oils used in processed foods. Visible fats include those foods that are solely or almost all fat, such as table spreads and cooking and salad oils. Invisible fats are those found in whole milk, eggs, meat and cheese.

The proportion of calories derived from fat in the average U.S. diet also increased during the same period, according to the Scientific Summary, since consumption of animal products has increased while consumption of cereal grains and potatoes, both low in fats, has decreased.

The institute acknowledged the public concern over recently raised questions as to the role of dietary fat in atherosclerosis and various forms of cancer. The report cited studies by various organizations and individual researchers on health effects, and noted that the dietary recommendations from these studies as well as those from other countries and organizations are in basic agreement on several points: that the diet should be made up of a variety of foodstuffs, that fats should be consumed in moderation, and that appropriate body weight should be maintained.

"At the same time," the IFT report concluded, "the high density of energy (calories) supplied by fats and oils contributes to the risk of obesity, and certainly moderation of their intake by those individuals at risk would seem well advised."

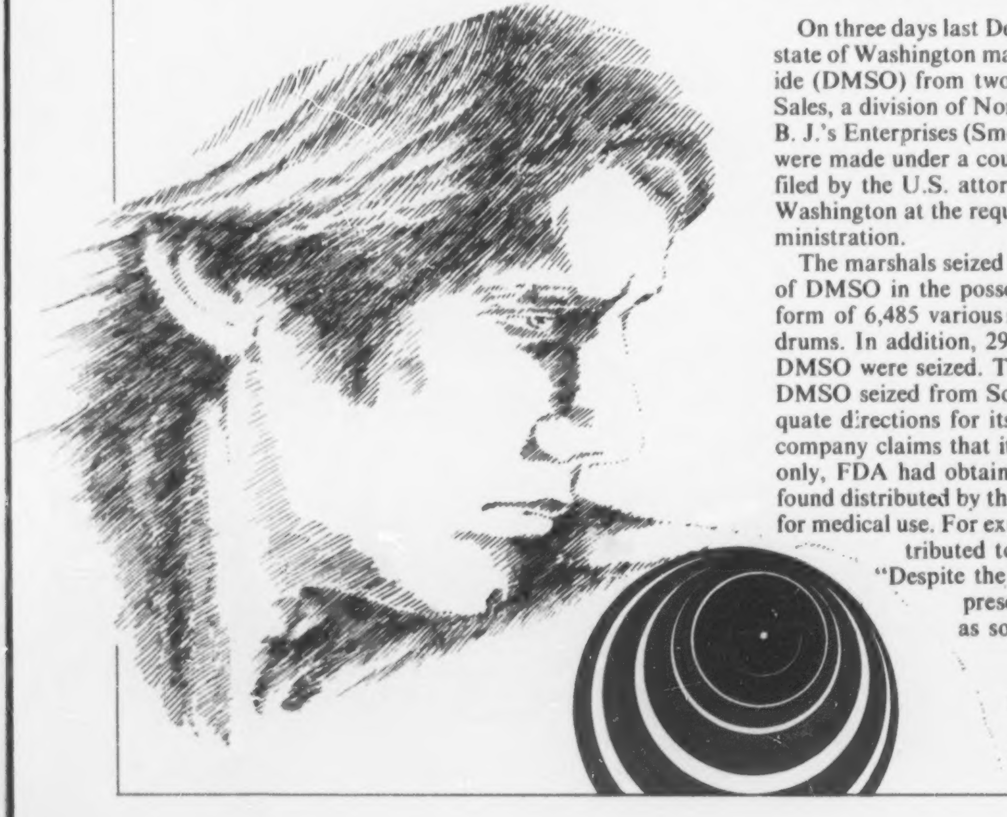
The Institute of Food Technologists is a professional scientific society devoted to the discovery and application of new and existing knowledge to improving the world's food supply. The Chicago-based institute has 20,000 members who are active in academic, industrial and government organizations.

What constitutes too much or too little fat in the diet was explained in the article "On Being Too Rich, Too Thin, Too Cholesterol Laden" in the July-August 1981 issue of *FDA Consumer.*

More DMSO Seized

On three days last December, U.S. marshals in the state of Washington made seizures of dimethyl sulfoxide (DMSO) from two area distributors, Solvent Sales, a division of Nordic Laboratories, Seattle, and B. J.'s Enterprises (Smoke Shop) in Fife. The seizures were made under a court order after complaints were filed by the U.S. attorney for the western district of Washington at the request of the Food and Drug Administration.

The marshals seized approximately $200,000 worth of DMSO in the possession of Solvent Sales in the form of 6,485 various size bottles and four 55-gallon drums. In addition, 29,366 empty bottles labeled for DMSO were seized. The complaint charged that the DMSO seized from Solvent Sales failed to bear adequate directions for its intended uses. Although the company claims that it is selling DMSO as a solvent only, FDA had obtained advertising and literature found distributed by the firm to promote the chemical for medical use. For example, a promotional piece distributed to prospective retailers stated: "Despite the fact that DMSO sold without prescription must be sold for use as solvent and disclaim all medical applications, let's be frank: the bulk of bottled DMSO is being used by your customers as a pain relief medication."



At B. J.'s Enterprises, the marshals seized 38 eight-ounce bottles of DMSO. The complaint filed by the government charged that DMSO distributed by B. J.'s is a "new drug" that has not been approved by FDA for marketing for the uses for which it is promoted by B. J.'s and that the drug labeling fails to bear adequate directions for use. The firm promoted the sale of its DMSO through use of a pamphlet, "Wonder Drug or Industrial Solvent? DMSO," which claims that DMSO is effective in the treatment of 34 conditions including cancer, gout, aortic aneurisms, burns, arthritis, baldness and herpes simplex.

These were the fourth and fifth seizures of DMSO intended for medical use. Earlier seizures were made in Buffalo, N.Y., Menominee, Wis., and Tampa, Fla. The history of DMSO was the subject of a short article titled "DMSO: No Proof of 'Miracles'," in the September 1980 *FDA Consumer*.

PPI Replacement

A Committee on Patient Education has been established within FDA to help educate consumers about prescription drugs. The committee was formed by FDA Commissioner Arthur Hull Hayes Jr., M.D., at the direction of Health and Human Services Secretary Richard S. Schweiker after a proposal to test patient package inserts (PPIs) for 10 drugs was rescinded.

The patient education committee will not only have a public education function but will also serve as a catalyst for private sector initiatives in this area. The PPI program was to be tested over a 3-year period.

Commenting on the committee and the PPI proposal, Secretary Schweiker and Commissioner Hayes said in a joint statement:

"This department remains committed to the need for patients to have more information about prescription drugs. Patients must actively participate with their physicians and others involved in health care in deciding on the best therapeutic approach to treating illnesses.

"The question is what is the best system, or systems, for providing that information. Our review of the 10-drug pilot program developed last year showed it to have significant limitations and to impose unreasonable constraints on the health care system. Moreover, we learned during our review that many physicians, pharmacists and other health professionals believe there are more effective and cost-efficient ways to bring information to consumers.

"We recognize that the government has an important and necessary role to play in consumer education about prescription drugs and other health care products and that the private sector has begun to take innovative and effective steps toward more patient information. These efforts need to be encouraged and supported by the government."

The functions of the Committee on Patient Education, to be chaired by Commissioner Hayes, are as follows:

—to identify new ways to bring information about prescription drugs to consumers.

—to encourage additional private sector initiatives.

—to work closely with health professionals on systems that will facilitate the providing of more information to patients.

—to evaluate existing patient information systems as well as new ones.

—to encourage the formation and to serve as a liaison for outside organizations that are or want to become active in patient information systems.

—to provide guidelines and serve as a clearinghouse for firms that want to draft prescription drug information.

—to alert consumers and health professionals to the usefulness and availability of prescription drug information.

—to assess the adequacy and effectiveness of private sector patient information systems and to provide to the secretary of HHS on a regular basis reports and recommendations.

—to identify the need for patient information in the use of other products regulated by FDA, such as medical devices, X-rays and biological products.

In addition to Dr. Hayes, the members of the committee are:

Mark Novitch, M.D., deputy commissioner, vice chairman; Robert Brady, executive assistant to the commissioner; J. Richard Crout, M.D., director, Bureau of Drugs; Jerome Halperin, deputy director, Bureau of Drugs; James Benson, deputy director, Bureau of Radiological Health; Victor Zafra, acting director, Bureau of Medical Devices; Harry Meyer, M.D., director, Bureau of Biologics; Thomas Scarlett, chief counsel; Michael Peskoe, associate chief counsel for drugs; Kenneth Durham, acting associate commissioner for policy coordination, executive secretary of the committee.

Also Stuart Nightingale, M.D., acting associate commissioner for health affairs; Gerald Barkdoll, associate commissioner for planning and evaluation; Alexander Grant, associate commissioner for consumer affairs; Robert Wetherell, associate commissioner for legislative affairs; Wayne Pines, associate commissioner for public affairs; Peter Rheinstein, M.D., director, division of drug advertising and labeling, Bureau of Drugs; Lloyd Millstein, Ph.D., deputy director, division of drug advertising and labeling, Bureau of Drugs; and Louis Morris, Ph.D., head, patient labeling branch, Bureau of Drugs.

FDA now requires PPIs for isoproterenol inhalation preparations, oral contraceptives, estrogen drugs used by menopausal and post-menopausal women and for drugs containing progestins. PPIs are also required to be given to women before they decide to use an IUD—an intrauterine contraceptive device. These PPIs are not affected by the December actions. Several articles on PPIs have appeared in *FDA Consumer*, the most recent being "Rx With a Dose of Info" in the November 1980 issue.

Angina Drug Approved

A new drug, nifedipine, has been approved by FDA. It is a potentially important alternative treatment for patients with angina—the vise-like chest pains that result when narrowed or contracting arteries starve the heart muscle of oxygen-bearing blood.

Dr. Arthur Hull Hayes Jr., FDA commissioner, said the approval represents a "significant medical advance for patients who cannot tolerate or are not helped by other drugs."

To be marketed by Pfizer Inc. of New York under the trade name Procardia, the drug is one of a new group of drugs called "calcium blockers." Calcium molecules play a role in causing the blood vessels to contract and narrow. By blocking this action, the drugs keep open the vessels supplying blood to the heart. Nifedipine is the first in the calcium blocker group to be approved in an oral dosage form.

Other drugs for angina are nitroglycerin, which has been used for more than a century, and beta blockers, which have been available since 1967 but which generally cannot be used for angina patients with asthma or weak hearts.

Nifedipine is not necessarily more effective than beta blockers but has a different mechanism of action and range of side effects. It may sometimes be useful as added therapy, although great care must be taken when used with other angina drugs, Dr. Hayes said.

FDA has approved one other calcium blocker, verapamil (marketed by Knoll as Isoptin and by G. D. Searle & Co. as Calan) as an injectable for emergency room use to calm irregular or rapid heartbeats known as arrhythmias.

Both old and new drugs to treat the symptoms of heart disease were described in the article "Drugs Are Dear to Many Hearts" in the December 1981-January 1982 issue of *FDA Consumer*.

Prison Drug Testing

FDA has proposed a new policy on the use of prisoners for drug and medical device research. Under the new proposal, published Dec. 18, 1981, FDA would accept the results of research other than that intended to directly improve the health of prisoners if the sponsor shows a need to use prisoners and meets other conditions. One key condition is that the prison environment permit prisoners to freely consent—or decline—to participate in the research. Local institutional review boards would be charged with ensuring that this condition is met.

Under an earlier version of the regulations only research aimed directly and specifically at improving the health of the prison population would have been accepted. Prisoners at the State Prison of Southern Michigan at Jackson had objected to this policy, saying it would end existing drug testing programs. Four of the prisoners filed suit in 1980 to block the regulation. The Upjohn Co. of Kalamazoo, Mich., which operates research facilities at the prison, joined in the suit.

The prisoners contended that they were protected by Michigan Department of Corrections policies from coercion and other abuses. Upjohn said research at Jackson was under careful medical supervision and was open only to prisoners who were fully informed volunteers.

The U.S. District Court for the Eastern District of Michigan in Detroit then dismissed the prisoners' suit after FDA agreed last June to take a new look at the regulation.

FDA believes the new proposal is in keeping with the recommendations of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. That commission was created by Congress under the National Research Act of 1974. The commission was concerned that crowding and promises of parole not be used to pressure prisoners, and sought to ensure that prisoners had grievance rights and contact with the public.

The final rule will become effective 90 days after publication in the *Federal Register* (FR Dec. 18, 1981).

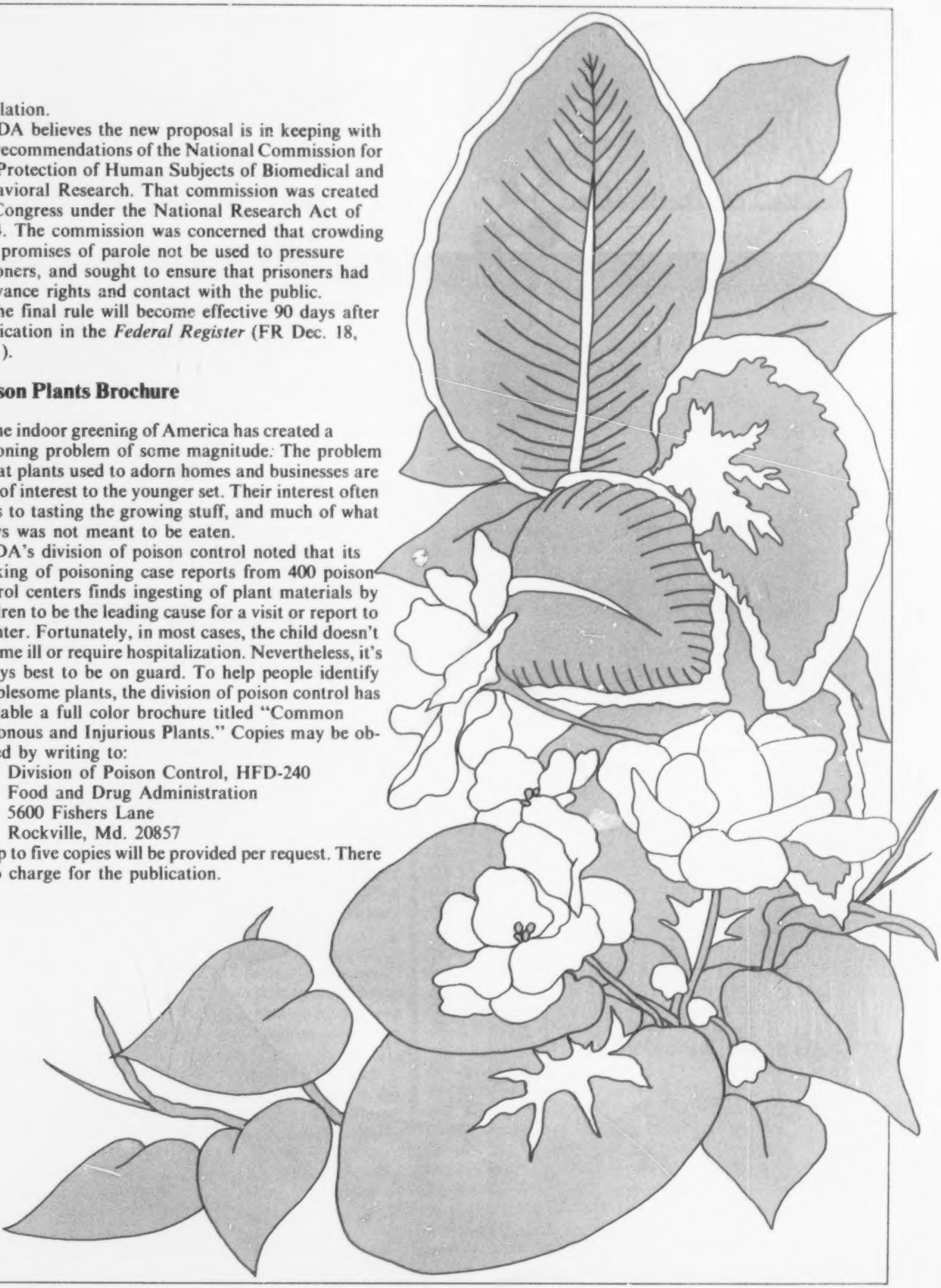
Poison Plants Brochure

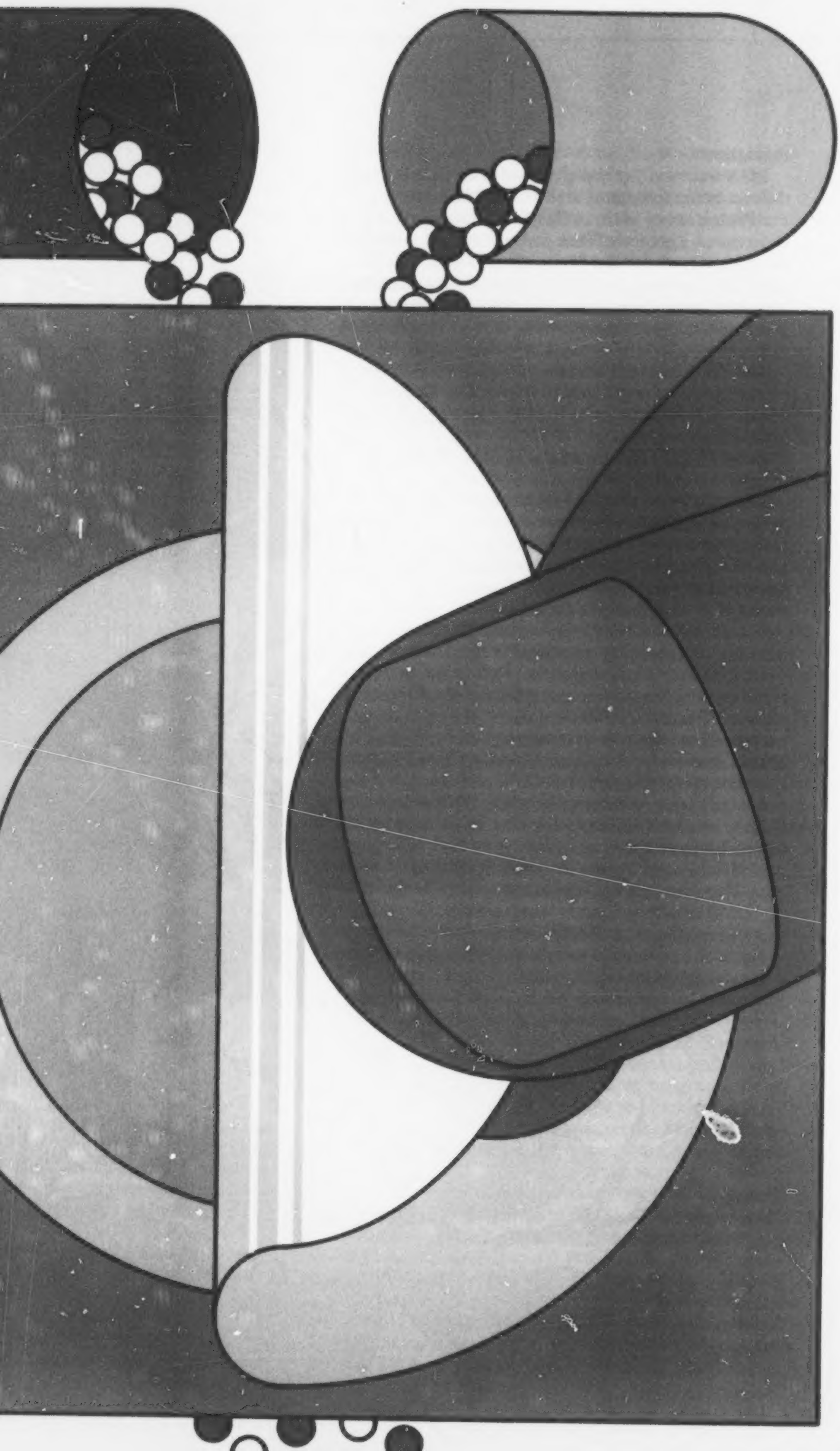
The indoor greening of America has created a poisoning problem of some magnitude. The problem is that plants used to adorn homes and businesses are also of interest to the younger set. Their interest often leads to tasting the growing stuff, and much of what grows was not meant to be eaten.

FDA's division of poison control noted that its tracking of poisoning case reports from 400 poison control centers finds ingesting of plant materials by children to be the leading cause for a visit or report to a center. Fortunately, in most cases, the child doesn't become ill or require hospitalization. Nevertheless, it's always best to be on guard. To help people identify troublesome plants, the division of poison control has available a full color brochure titled "Common Poisonous and Injurious Plants." Copies may be obtained by writing to:

Division of Poison Control, HFD-240
Food and Drug Administration
5600 Fishers Lane
Rockville, Md. 20857

Up to five copies will be provided per request. There is no charge for the publication.





New Routes For Drugs To Travel

by Annabel Hecht

Anyone suggesting that some day drugs might be directed to specific sites inside the body by magnets on the outside or that miniature pumps could course through the digestive system and release a steady stream of medication as they go might reasonably be accused of spending too much time curled up with Ripley's "Believe It Or Not."

Such unique ways of getting drugs to the right place inside the patient are not as far out as they may seem. In fact, a number of drugs in unusual packages already have been approved by FDA. They were developed because present-day drug dosage forms don't always deliver.

Drugs, as most people know them, come in many forms and shapes. There are tablets and capsules to be swallowed and there are tablets that are to be dissolved under the tongue. Liquids, both colorful and flavorful, help the medicine go down, especially when the patient is a tiny tot. Then there are aerosol sprays that send drugs up the nose or down into the lungs, creams and ointments to be rubbed on the skin, drops for the eyes, and solutions that are injected into a vein or muscle.

Despite this variety, drug taking has its problems. An oral dose usually provides a high level of the drug in the blood right away, but as the drug is eliminated from the body, the level of the medication in the blood drops. Another dose shoots the level up again. What results is roller coaster therapy. If the patient should skip a dose, the amount of drug in the system might drop dangerously low—a serious situation if the drug was being taken to prevent a condition such as irregularities of the heart beat.

Some drugs are eliminated from the body so fast that the patient has to take them frequently to be sure there is enough medicine in the system to do its job. This may become such a burden that the patient sometimes just doesn't bother or may forget to open that bottle of pills.

Many drugs produce unpleasant side effects; some are poorly absorbed if there is food in the patient's stomach. Powerful drugs used to treat cancer often damage healthy as well as disease cells. Injecting drugs in a vein or muscle can cause pain and discomfort and possible infection where the needle enters the skin.

Some of these problems have been overcome by "controlled release" dosage forms that became prevalent in the late 1950s. Such forms have a number of aliases including delayed action, repeat action, slow release, prolonged release and timed release forms.

Perhaps the most familiar is the widely advertised over-the-counter drug capsule containing hundreds of "tiny time pills." Variations in the thickness of the coating on each pill determines when the active ingredient will be released. In another form, the drug is divided between an outer layer that gives the first burst of medication and inner core protected by a waxy coating designed to release the rest of the drug six hours after it has been taken. Still another form is a tiny wax basket through which the drug diffuses gradually over a period of time. The basket itself remains intact until excreted.

In addition to controlled release drugs taken orally, there are pellets containing hormones that are implanted under the skin. Used to treat hormone deficiency diseases and some types of cancer, these implants release their medication over periods of several months while being absorbed into the tissues. One unusual, if not bizarre, approach to drug implantation started in 1955 when a French researcher developed a technique for implanting tablets of disulfiram under the skin of patients being treated for alcoholism. Disulfiram (trade name Antabuse) reacts with alcohol and makes the person who mixes drug and drink ill. The ease with which alcoholics could circumvent their treatment, by not taking the drug orally, was what led the researchers literally to sew the pills into the patient. The technique has never caught on in the United States.

One of the oldest controlled-release dosage forms is the tablet that is coated to assure that absorption takes place in the intestines rather than in the stomach. Enteric coating, as it is called, dates back to 1884.

Nearly 80 years after that early effort to control drug release an entirely new approach to achieve this end began to evolve—the concept that drugs would diffuse at a steady rate from implantable polymer containers. A polymer is a plastic-like material, similar to the synthetic fabrics from which clothing is made. Drs. Judah Folkman and David M. Long, then with the National Naval Medical Center in Bethesda, Md., are usually credited with the idea of using containers to control drug release. The two observed that thyroid hormone placed in a very small silicone rubber capsule was released at a steady rate day after day in a laboratory dish. The same steady release also occurred when the capsule was implanted in the heart muscle of dogs. After publication of their findings in 1964 other researchers demonstrated that a variety of drugs would diffuse through similar capsules over long periods of time.

Unfortunately, the silicone rubber capsule has one drawback—fat-soluble drugs of small molecular structure can't pass through it. Therefore, researchers in the late 1960s and early 1970s sought a material that would let larger molecules through without causing inflammation of the tissues. The perfect material—a polymer called ethylene-vinyl acetate copolymer—was found by Dr. Robert Langer of the Massachusetts Institute of Technology and Folkman, now with Harvard Medical School. They made the discovery while studying a substance that stops the growth of capillaries into certain tumors.

Three basic types of implantable drug release systems have resulted from research with polymers. They are:

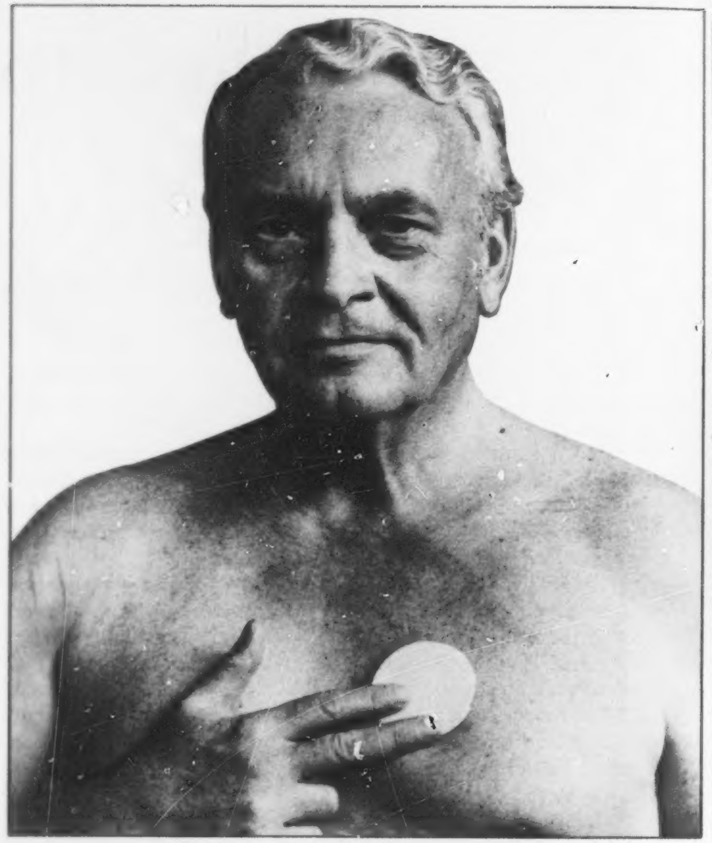
- The swelling system in which the drug is completely surrounded by a polymer. The polymer swells allowing the drug to migrate into the tissues.
- The chemical system in which the drug is dispersed throughout the polymer. The drug is freed to do its job when the polymer dissolves or erodes.
- Diffusion systems from which the drug migrates from within a polymer to the outer surface. The drug can be stored in a reservoir or dispersed throughout a polymeric matrix.

One unusual drug system, called OROS, uses polymers in an oral dosage form. Although it looks like a conventional tablet, OROS is actually a miniature osmotic pump. It consists of a drug reservoir, a surrounding semipermeable polymer membrane with a minute opening through which the drug is released. As it goes through the intestines, water enters through the membrane, gradually dissolving the solid core of drug. The internal pressure generated by the water then forces the solution out of the tiny hole in the capsule. Not yet on the market, the OROS system, developed by Alza Corp., is being tested with major drugs by several companies.

Unusual containers for controlled release systems have not been limited to polymers. Researchers throughout the world have been encasing drugs in tiny packages through the process known as microencapsulation. Microcapsules used in pharmaceutical research are measured in microns, a micron being one millionth of a meter (a meter is 39.37 inches). These incredibly small containers have been made of materials such as nylon and ethylcellulose and natural substances including albumin and liposomes. The substances encapsulated in them have included enzymes, hormones, cancer drugs, antigens, pentobarbital sodium and phenothiazines. Even red blood cells are being tapped to serve as microcapsules to carry corticosteroids and anti-cancer drugs.

Because of their extremely small size microencapsulated drugs can be injected into the subject and even manipulated once inside. A Chicago research team mixed ultrafine magnetic particles with a drug in an albumin microsphere (a microsphere differs from a microcapsule in that the drug is mixed with the polymer or other material instead of being surrounded by it). When the microspheres were injected into a rat's tail, the researchers were able to move them to the desired site by moving a magnet outside the animal's body. Another investigator has found he can increase the amount of drug released by passing a magnet over an implanted polymer matrix in which tiny magnetic steel beads have been embedded along with an active drug.

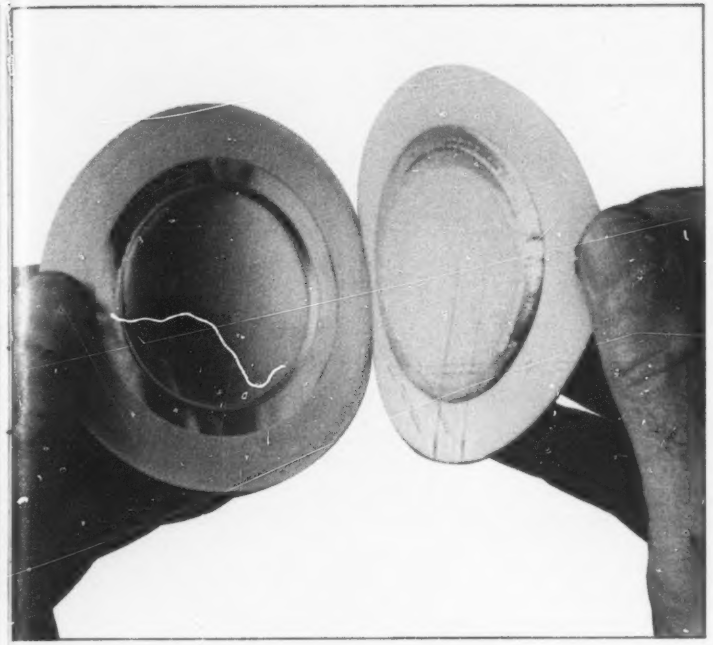
Although much remains to be learned about these unusual drug delivery systems, some of the principles behind them have been applied to products now on the market. The first of this new breed to get FDA approval was the Ocusert system for the treatment of glaucoma. The usual treatment for this eye disease calls for drops containing pilocarpine to be put in the eyes three or four times a day. Not only is this inconvenient, but there always is the chance that too little or too much of the drug will reach its target. The Ocusert system, consisting of two transparent membranes of ethylene-vinyl acetate copolymer with a reservoir of pilocarpine in between, is placed under the lower eyelid where it releases a steady dose of drug for about a week. The advantages of the Ocusert are obvious: It simplifies the glaucoma patient's drug-taking schedule, reduces the temporary blurring associated with the eyedrops and exposes the patient to less of the drug with the same effect. Ocusert was developed by Alza Corp. and is marketed by Ciba.



Another implantable slow release drug product is the Progestasert Intrauterine Progesterone Contraceptive System, also developed by Alza. In this system precisely controlled amounts of progesterone are released from a polymer reservoir in the long bar of a T-shaped device inserted within the uterus. The amount of progesterone delivered in the device's one-year life span is said to be equivalent to that contained in only three oral contraceptive pills.

Drugs don't always have to be taken internally to do their work; some can reach their target transdermally or through the skin. One such skin-delivery system is the Transderm-V, again developed by Alza, which is an easy way to take scopolamine for motion sickness. Oral scopolamine is effective but has many side effects. Transderm-V is a tiny, thumbnail size disc made up of an outer layer of polyester film, a reservoir to hold the drug, a polypropylene membrane that controls the release of the drug, and an adhesive layer to hold the disc in place behind the ear.

The system provides enough scopolamine for three days and is claimed to reduce some of the side effects usually associated with this drug. Some reports, however, indicate that side effects such as dryness of the mouth, drowsiness and blurred vision do occur with the transdermally delivered scopolamine.



Placed on the chest or upper arm, Searle's NITRODISC *consists of an adhesive pad containing nitrogen, which is used for angina (chest pain) attacks. The medication is fed uniformly through the skin over a 24-hour period.*

FDA has given provisional approval to three similar drug systems that deliver nitroglycerin through the skin. Nitroglycerin is the primary treatment for angina, the chest pain that comes when the heart is deprived of oxygen. Usually the patient dissolves a nitroglycerin tablet under the tongue when the pain occurs. Since the effect lasts only about 15 minutes, many pills may have to be taken during the course of a day. With all three new drug systems, a whole day's supply of nitroglycerin is contained in a single adhesive bandage that is applied to the chest or upper arm.

In one of these systems, the Nitrodisc, developed by G. D. Searle Co., the drug is dispersed throughout a polymer in tiny microcompartments. These compartments serve as tiny reservoirs from which the nitroglycerin is diffused into the skin at a steady rate. The Nitro-Dur system of Key Pharmaceuticals Inc. contains a number of chemical binding sites distributed throughout a three-dimensional polymeric matrix. Nitroglycerin molecules bound to these sites gradually dissolve into a fluid phase, which then permeates the skin. The third system, Alza's Transderm-Nitro, is a four-layer disc consisting of an outside layer impermeable to nitroglycerin, a drug reservoir containing the nitroglycerin, a membrane through which the drug will diffuse, plus a layer of silicone adhesive to hold the disc in place.

While drugs in these transdermal systems reach their site of action through the bloodstream, direct delivery to the spot where the drug is needed is the concept behind the INFUSAID, an implantable pump soon to be approved by FDA. In contrast to the microcapsules and microspheres of some controlled-release drugs, INFUSAID is about the size of a hockey puck and is implanted in the patient's abdomen. The pump is a disc made of titanium, divided inside into two chambers by a bellows. The bottom compartment contains a fluorocarbon propellant that exerts a constant pressure against the bellows. The drug, in the upper chamber, is pushed by the propellant into a catheter that is inserted into a vein or an artery. The upper chamber can be refilled as needed by means of a hypodermic syringe without discomfort to the patient.

Developed at the University of Michigan Medical Center, INFUSAID was originally designed to infuse heparin, a blood thinning drug, into patients with severe blood clotting problems. It has now been adapted to deliver powerful cancer drugs directly into the hepatic artery to treat liver tumors. The infusion pump not only is prolonging the lives of victims of liver cancer, but is making those years better in a number of ways. For instance, toxic drugs are confined to the malignant cells rather than being dispersed throughout the body, thus keeping side effects to a minimum. In addition, the patient does not need to be hospitalized and can pretty well carry on a normal life.

Infusion pumps, transdermal systems and polymer capsules might be just the tip of the iceberg. Interest in controlled release delivery systems is high not only in the pharmaceutical industry, but also in university laboratories. What new and unique systems will result is anybody's guess.

Microencapsulation of drugs to release them at target sites is viewed as one of the emerging technologies that will need FDA's attention in the next five or so years, according to a survey of a group of 190 scientists within and outside the agency.

Scientists studying polymers see their potential for the sustained release of insulin, heparin, growth hormone, interferon and other potent macromolecules produced by the body.

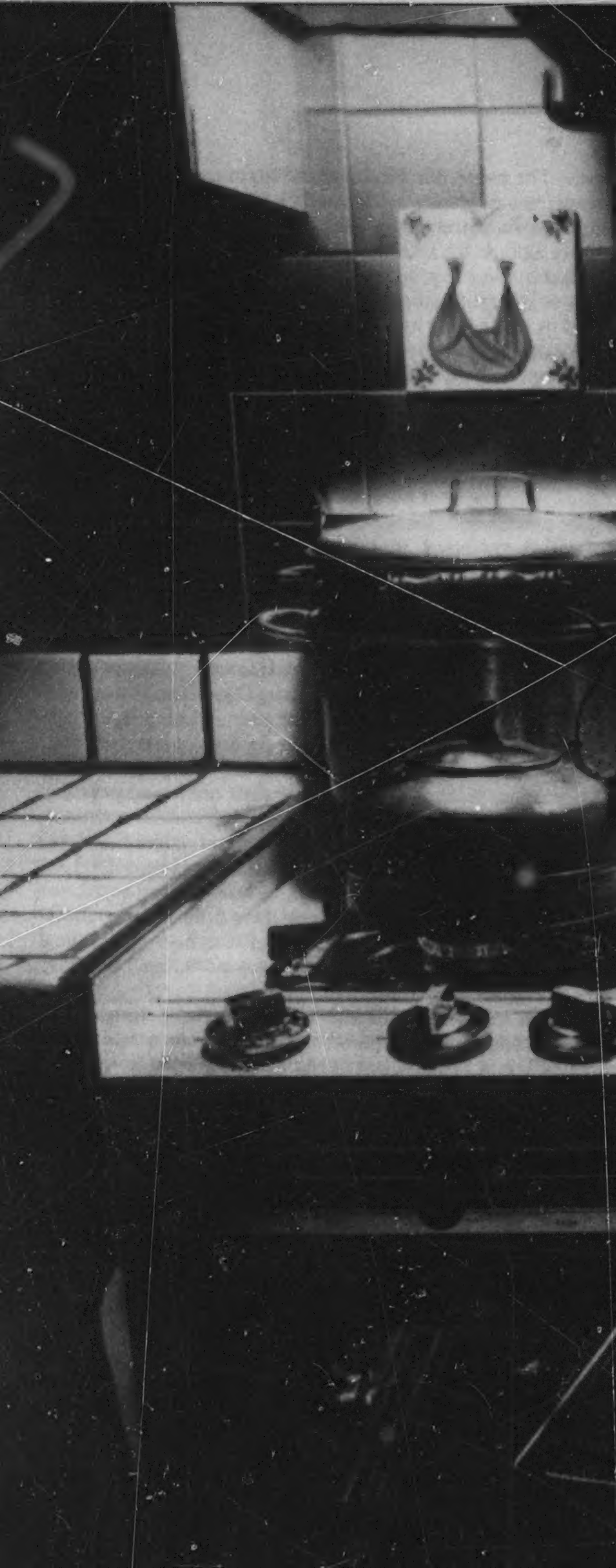
The next major breakthrough in infusion pump design may be a closed-loop infusion system, according to a recent report to FDA. In such a system the patient's need for a drug will automatically trigger the release of an appropriate amount.

Whatever is developed, be it drug or device, any new delivery system is subject to FDA scrutiny. However, most controlled release preparations are simply old drugs in a new dress. Since the safety and effectiveness of the original dosage form of these products has been established, manufacturers usually are not required to carry out large controlled clinical tests. They do have to provide bioavailability data to show that the product meets the controlled release claims made for it; that it is designed to prevent dose dumping—that is, the active ingredient is not released all at one time; that its effect is the same as approved conventional dose forms or controlled release forms containing the same active ingredients; and that each individual dose behaves in the same way.

Drugs marketed for the first time in controlled release form do need to be tested for safety and effectiveness.

Devices that are implanted in the patient must be approved before they go on the market and, of course, must be shown to be safe and effective. In some cases the manufacturer may be required to monitor patients for certain periods of time after the device is put inside to make certain no problems develop.

Annabel Hecht is a member of FDA's public affairs staff.



CALORIC

COOKWARE As A Source Of ADDITIVES

by Doug Henderson

The truly discriminating gourmet cook with a healthy supply of cash can purchase a 10-inch silver frying pan from Tiffany and Co. of New York City for $1,675. One would be hard-pressed to label that a bargain. But consider that silver is the number one metal for conducting heat, and consider how much class a silver skillet would add to the pegboard on almost any kitchen wall.

Fortunately, there are affordable alternatives: copper, aluminum, iron, stainless steel, glass and pottery, to name a few. In general, FDA considers food prepared in these cookware alternatives to be safe, although questions have been raised by consumers about the safety of cooking utensils made of some metals, particularly cookware made of aluminum and copper, and pottery coated with lead glaze.

Some of the questions: Does metal from aluminum cookware ever get into our food in dangerous amounts? Are there precautions that should be taken when cooking with copper? Is there a problem with cooking or holding foods in pottery coated with glazes that contain lead?

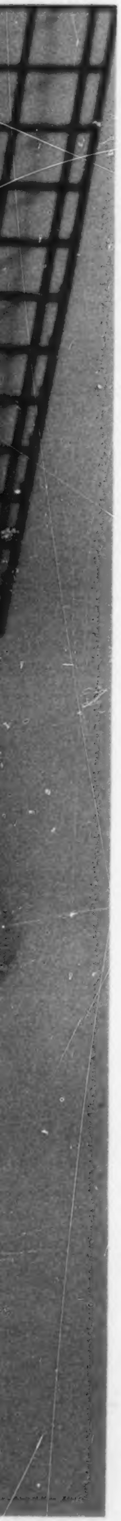
FDA's responsibility for the safety of our food supply extends to the safety of metals in cookware because of the possibility that some metals may leach into food in amounts large enough to be potentially harmful. To leach means to dissolve and wash into. Under the law, any food is considered adulterated "if it bears or contains any poisonous or deleterious substance which may render it injurious to health." Products that are found hazardous by FDA are subject to immediate removal from the market.

Increased public concern has focused on aluminum since July 17, 1980, when, in a letter to the highly regarded *New England Journal of Medicine*, Dr. Stephen Levick of the Yale University School of Medicine hypothesized a connection between the use of cheap aluminum cookware and Alzheimer's disease, a progressive brain disorder characterized by memory loss and learning deficiencies.

Levick wrote that as a "financially strapped medical student," he had purchased inexpensive aluminum pots and pans. After two years of use, he noticed "corrosive pitting and whitish powdery deposits around the pots." Afterward he learned that in Alzheimer's disease, higher than normal levels of aluminum had been found in the brain tissue of deceased victims. Levick then suggested a possible connection between Alzheimer's disease and the ingestion of aluminum, but expressed the belief that his hypothesis required more systematic study. In the meantime, he said, he would no longer use his cheap aluminum pots.

Levick made no reference to a 1980 study which showed that autopsies of Alzheimer patients revealed slightly lower levels of aluminum in their brains than were found in autopsies of normal adults. There were also greater levels of mercury in the brain tissues of these victims as compared to normal adults. Nor did Levick mention that scientists remain puzzled over a major question concerning the concentrations of aluminum in brain tissue from Alzheimer patients: Does aluminum ac-

Club



cumulation in the brain cause the disease or does the disease itself alter body chemistry to allow accumulation of aluminum? According to FDA officials, no direct causative effect between aluminum and Alzheimer's disease has been shown to date.

Does the ingestion of aluminum in the diet, either that naturally present in food or added from aluminum cookware, pose any other human health hazard? While a portion of any ingested aluminum is absorbed into the body through the gastrointestinal tract, the total amount is far less than that which could be expected to result in any adverse health effects. A large percentage of the aluminum ingested is excreted along with other waste material.

When one cooks with aluminum, does it migrate into the food? Under normal conditions the total amount of aluminum added to food from cookware is relatively small. However, prolonged retention in aluminum cookware (from five or six hours to several days) of certain highly acidic foods such as tomato sauce, sauerkraut or beverages including citrus juices and carbonated drinks may cause more aluminum than usual to enter the food. Similarly, higher levels of aluminum will migrate into acidic or salty foods stored in aluminum foil. Because metallic aluminum is subject to some disintegration from salt or acid foods, white powdery deposits may accumulate on the aluminum foil or it may even develop pinholes after extended contact with such foods. However, there is no conclusive evidence showing toxic symptoms from consuming acidic or salty foods, either cooked in aluminum pans or stored in aluminum foil.

Many aluminum compounds are sanctioned by FDA for use as buffering agents (acid neutralizers) in antacids, bleaching agents in cheeses, leavening agents in bread and flour and mordants (color fixers) in some coloring agents. Such approval has been based on a number of studies that have demonstrated the relative safety of these aluminum compounds at the present levels of use.

Copper is called a "noble" metal by cooks and chemists, but for different reasons. Noble to a chemist means that the metal does not corrode easily. To a cook or an ordinary layman, it means magnificent in appearance. To both, copper fills the bill.

Copper is also an excellent conductor of heat (second only to silver); hence its wide use in the kitchen. Cooks often prefer copper cookware, particularly for delicate sauces and foods that must be cooked at precisely controlled temperatures.

Most copper cookware is lined with tin and presents no problem of copper migration into food, although the pan must be relined when the tin starts wearing thin. Using unlined copper utensils for cooking or storing food may be harmful. Copper migrates to any food with which it comes in contact, especially those high in acid. An essential nutrient in the body, copper aids in the absorption and metabolism of iron. But copper can be toxic at much lower levels than aluminum. Those persons who ingest food containing harmful levels of copper may experience nausea, vomiting or diarrhea. Thus FDA recommends that consumers use only tin lined copper cooking utensils for cooking or storing food.

There are many types of enameled, ceramic and glass cookware. Generally, they present no safety problems. For example, in the United States the enamels applied to the food contact surfaces of iron or steel cookware do not contain lead or cadmium. When enamels containing lead or cadmium or both are applied to aluminum vessels, they are not applied to the food contact surfaces. Therefore porcelain-enameled cookware so manufactured does not represent a potential problem.

But some foreign manufacturers at one time decorated the interior of metal cookware (including the lids) with brightly colored cadmium-containing enamels. As a result of this practice, a number of shipments were denied entry into the United States. However, this practice was discontinued in the early 1970s.

Glass and glass ceramic ware should be perfectly safe to use. The manufacturing process for these products is such that they are of no concern.

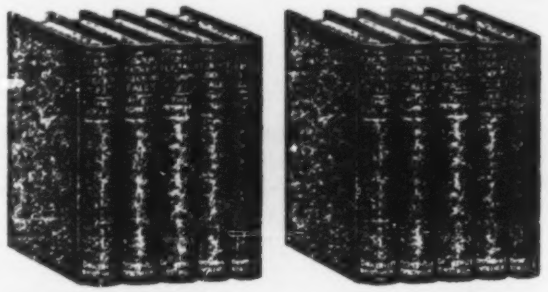
China, crockery and earthenware are also forms of ceramic cookware. If glazes used on them are improperly formulated, applied and fired, a health hazard might ensue because of the conditions of use. Acids from foods can react with such products and cause potentially hazardous levels of lead and cadmium to leach into food.

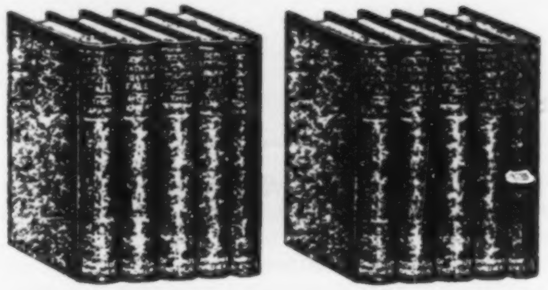
Fortunately, quality control standards for the ceramics industry have been made stringent as a result of concentrated efforts by FDA to educate industry about lead and cadmium migration problems. As a result, industry has implemented its own surveillance programs. Reputable domestic and foreign manufacturers now use correct firing and mixing methods to prevent lead and cadmium leaching problems. FDA continues to survey and obtain samples to assure continued safety of these products.

While efforts have been under way to educate the art potter and hobbyist concerning these potential problems, some amateur potters may be unaware of correct mixing and firing procedures. Therefore, it may be prudent to use such products for decorative purposes instead of for cooking and storing foods.

Doug Henderson is a technical writer in FDA's Bureau of Foods.

Diet Books Sell Well But . . .





by Judith Willis

Hope springs eternal not only in the human breast, but also, it seems, in the human stomach.

The person with a tummy that likes yummies yearns to feel full yet look flat. The human appetite hungers for some magic formula that allows eating abundantly at the same time that excess weight is being shed.

Increasingly in the last few decades, Americans have become more aware of the health consequences of being overweight and have come to consider an ideal body weight that sometimes seems on the emaciated side. The new diet—almost any new diet—turns up again and again as the focus of magazine articles and best selling books.

Scanning the popular literature for help in losing weight, the would-be dieter receives a confusing array of advice:

- Eat mostly protein foods and few, if any, carbohydrates.
- Consume an abundance of carbohydrates and little protein.
- Eat only rice—only ice cream—or only fruit.

One diet expert may advise eating only twice a day. Another proposes six meals a day, a third says eat as often as you like.

How are 50 million overweight Americans to sort it all out? How can they (and other millions who are not clinically overweight but who desire to be thinner) select a diet that will help them lose weight but not jeopardize their health?

Many dieters have asked FDA's advice about the various diets. FDA is responsible for the safety of foods and their appropriate labeling. But claims made in new articles and books for foods or dietary regimens are generally out of FDA's domain. In fact, such claims are protected under the First Amendment to the Constitution. This means that anyone, regardless of nutritional or medical expertise, can make any claims he wishes in articles or books. However, if a book or article is used to misbrand a particular food, its use may be regulated by FDA.

Consumers, then, need to protect themselves from diets that could be harmful. One way to do this is to consult a physician before embarking on any diet, and if possible, consult a dietitian or nutritionist as well. Consumers can also inform themselves about the basics of nutrition to understand the risks associated with specific diets and to discount the extravagant claims and unscientific reasoning put forward for some of them.

A concept essential to dieting is that of the calorie. Most promoters of diets consider reducing one's intake of calories essential to loss of weight. But there are some "experts" who claim that "calories don't count" or that some calories, for example calories from protein, are different from calories from carbohydrates.

Who is right?

A calorie is a measure of heat energy. One calorie (known technically as a kilocalorie) is the amount of heat it takes to raise the temperature of a kilogram (about a quart) of water by 1 degree Celsius. Therefore, it doesn't matter whether this energy is generated by protein, carbohydrate or fat, so long as it raises the temperature of a kilogram of water that 1 degree. The misconception about different types of calories may arise because different food nutrients provide different numbers of calories on a per gram basis: Carbohydrate and protein each supply four calories per gram, fat provides nine and alcohol eight. (There are 28.4 grams in an ounce.)

The human body requires a certain number of calories each day to maintain its weight. The number varies with age, body size and activity. For each pound a dieter wishes to lose, he or she must cut out the necessary number of calories from the diet, or increase physical activity to burn these excess calories.

It takes 3,500 calories to burn a pound of body fat stored in the tissue. To lose one pound of fat a week, a person must either reduce food consumption by 500 calories a day, or expend enough energy to burn 500 calories a day more, or an appropriate combination of the two.

Advocates of some diets claim their plans will make it possible to lose weight at a faster rate, or at a higher caloric intake than other diets permit. This claim is often made for high protein, low carbohydrate diets. In *The Doctor's Quick Weight Loss Diet,* Irwin Maxwell Stillman claims that his high protein (virtually no carbohydrates) diet will cause the "system to burn more calories daily than with a diet of the same total caloric intake that includes other foods." He explains that fat is burned at a quicker rate on an "unbalanced" high protein diet than on a balanced diet.

The rationale for this claim is based on the concept of ketosis. Energy is obtained primarily from the breakdown of fat. Ketosis is a process that occurs when a person's diet is so low in carbohydrates that the fat deposits are broken down for energy faster than the body can use them. Ketone bodies are formed from the incomplete breakdown of fatty acids. In ketosis, the ketone bodies accumulate. This can lead to an acid and alkaline imbalance in the body. Because the excess ketones must be excreted into the urine, the dieter on a low calorie, high protein, low carbohydrate diet gets rid of large amounts of water. This shows up as a quick and substantial weight loss. Ketogenic diets, therefore, require a large intake of water and other fluids to make sure that the body has enough fluid to rid itself of the ketones and to keep the dieter from becoming dangerously dehydrated. Because most of the loss is water, not body fat, many dieters find that much of the weight loss from this type of diet is regained soon after normal eating is resumed.

Another physiological fact to consider before embarking on a ketogenic diet is that in ketosis the body's mode of burning calories may be similar to that of fasting. The body's fuel comes from glucose, which is most easily obtained from carbohydrates and less easily from protein. When the body lacks carbohydrates, as when a person is fasting or is on a low calorie and very low carbohydrate diet, protein is degraded to supply the minimum level of glucose. This protein is taken from lean body mass muscles and major organs such as the liver, heart and kidneys.

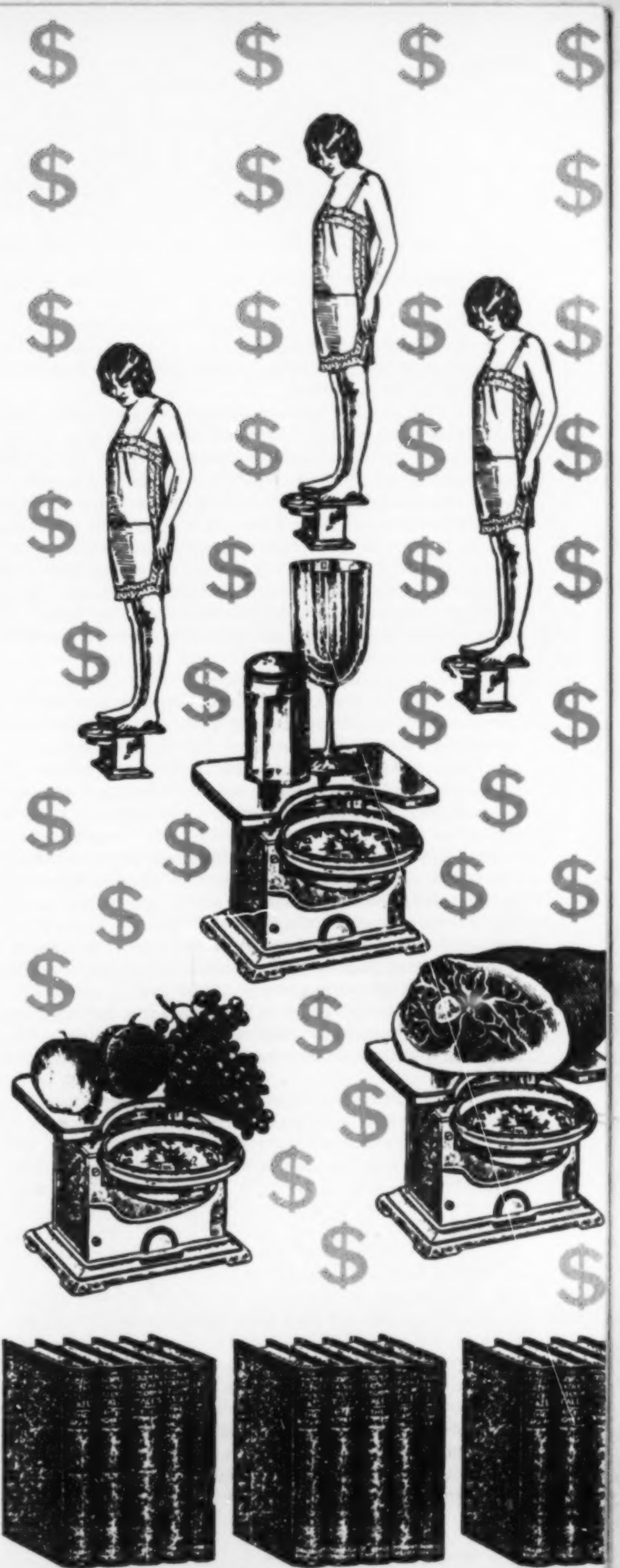
This is primarily the reason for the rather dramatic initial weight loss in low calorie, high protein diets. While 3,500 calories are needed to burn a pound of body fat, it takes only 480 calories to get rid of a pound of "lean body mass."

Another ketogenic regimen is a very low calorie (fewer than 400 calories) protein diet, particularly the liquid protein diet. These diets have been associated with deaths resulting from ventricular arrhythmia (irregular heart rhythms) in 17 relatively young healthy persons, according to a team of investigators from FDA and the Centers for Disease Control. As a result of their study, published in the April 1981 issue of *The American Journal of Clinical Nutrition,* this team recommended that the use of these weight reduction programs be curtailed until scientists can find out how, or even if, they can be made safe.

The 17 deaths were among a number of deaths of dieters following very low calorie protein regimens. Some of the victims had underlying diseases that could have caused their deaths; however, these 17 dieters were free of serious underlying disease and their deaths had no apparent cause. The 16 women and one man all took vitamin or vitamin-mineral supplements while on the protein diets. Of these, 12 were dieting under medical supervision. All 17 patients died suddenly, some in the hospital. Cardiac arrest occurred in five patients before they were hospitalized. None of the five ever regained consciousness. Extremely rapid heartbeats and erratic heart functioning were documented in 11 people who died under observation.

Because of these deaths, FDA has pending a regulation to require warning labels on products for weight reduction (especially those intended for use as the sole source of nourishment) if more than 50 percent of the calories they contain comes from protein. The agency also is currently investigating several acute illnesses requiring hospitalizations associated with the Cambridge Diet, a 330-calorie-a-day plan in which a powder is mixed with liquid. In this product, less than 50 percent of its calories comes from protein.

Ketogenic diets not only include liquid protein diets (e.g., Robert Linn's Last Chance Diet) but also diets that consist



almost entirely of protein in the form of solid foods such as meat, fish, poultry and eggs (e.g., Irwin Maxwell Stillman's Doctor's Quick Weight Loss Diet, Robert Atkin's Diet Revolution), and high protein diets in which carbohydrates are allowed at a low level (e.g., Baker and Tarnower's Scarsdale Medical Diet).

Almost the exact opposite of the high protein diet is a food plan published recently by Nathan Pritikin. Pritikin says his diet plan is primarily aimed at the prevention or treatment of high blood pressure, diabetes, gout, atherosclerosis, gallstones and other diseases. However, it also includes a weight loss plan that is a 1,000 calorie diet with protein intake limited to 10 percent to 15 percent and meat limited to less than a quarter pound daily. It is high in complex carbohydrates (whole grains, fruits and vegetables) and low in fats (5 percent to 10 percent), cholesterol and highly refined carbohydrates such as sugars. Salt is restricted, and coffee, tea and alcohol are not allowed.

The scientific community appears to be divided in its assessment of the Pritikin plan. Some see it as nutritionally sound and useful. Others, such as Elizabeth M. Whelan of the American Council on Science and Health, criticize it as restrictive, austere and dreary. The American Medical Association questions the safety and effectiveness of the plan, especially for the diseases it is supposed to help prevent. In a November 1981 news release, the AMA said that researchers at the University of Alberta in Canada had reason to believe that the program offered no more relief from peripheral vascular disease (disease of blood vessels outside the heart) than did the more moderate American Heart Association diet combined with exercise. The AMA said that researchers further reported that the Pritikin plan, because of its lower fat and protein intake requirements, might lead to reduced resistance to infection and poor wound healing. The lower intake of calcium and iron may also make it unsuitable for pregnant women and other women of childbearing age, the AMA said.

Just as the Pritikin plan seems to be in agreement with a contemporary shift in nutritional emphasis from proteins to complex carbohydrates, so originators of diets in the past few years seem to have kept in step with health concerns of their times. For example, in the early 1960s, the rising concern with the avoidance of saturated fat seems to have given credence to a ketogenic diet espoused by Dr. Herman Taller in the book Calories Don't Count. Taller theorized that the number of calories a person consumes doesn't matter, and that "the calories of carbohydrate and the calories of unsaturated vegetable oil work quite differently in the system." His convoluted, unproven theories revolved around the tenet that a person had to eat polyunsaturated fats to be slim. Because the book was being sold in stores alongside capsules of safflower oil, FDA instituted proceedings charging violation of drug regulations against Taller, who was also convicted of mail fraud and conspiracy.

Another approach taken by some diets is that a certain food somehow burns calories to get rid of fat. One version of this is the grapefruit diet in which dieters are instructed to eat grapefruit before each meal and then literally stuff themselves with as much bacon, eggs, meat, fish and vegetables as they like. The diet is based on the erroneous theory that grapefruit contains enzymes that somehow subtract calories by increasing the fat-burning process. The diet is often called the "Mayo Diet," although the famed Mayo Clinic in Rochester, Minn., steadfastly denies any association with it.

A recent entry into the weight loss sweepstakes is the fructose diet, which capitalizes on the current interest in fructose as an alternative to table sugar (sucrose—half fructose, half glucose). The Fabulous 14-day Fructose Diet is a ketogenic, low carbohydrate, high protein diet that provides approximately 700 to 1,000 calories a day. About 150 of those calories are from fructose.

Another recent and enormously successful weight loss program is Judy Mazel's Beverly Hills Diet book, which was No. 1 on the *New York Times* non-fiction best seller list for several weeks in the fall of 1981.

Like other diet hits of the past, it combines sound health advice, such as limiting sodium, with trendy ideas such as the use of bran, sesame seeds, brewer's yeast and raw butter. Basically, the Beverly Hills Diet is a low calorie fruit diet. For the first week the dieter eats only pineapples, bananas, papayas, mangos, strawberries, apricots, blueberries, watermelon, apples and prunes.

It is not until the 11th day of the diet that something other than fruit is allowed (bagels, butter and corn on the cob), and it is not until the 19th day that a significant source of protein (steak or lobster) is permitted. Then, through the fifth week, protein foods are allowed only one day a week.

The Beverly Hills Diet is based on the false theory that protein and carbohydrate digestive enzymes cannot work together and that while protein enzymes are needed to digest protein, and carbohydrate enzymes for carbohydrates, fruit does not need the body's enzymes to be digested because it has its own enzymes. Another unfounded claim made by Mazel is that the enzymes in fruit can render other foods less fattening.

"Fat," Mazel says, "means. . . undigested food . . . . When your body doesn't process food, doesn't digest it, that food turns to fat."

Mazel claims that in order to digest food properly, a process she calls "conscious combining" must be used. Her rules of conscious combining call for eating proteins only with other proteins, and fats and carbohydrates only with other carbohydrates and fats. Fruits are to be eaten alone. Because of the supposed enzymatic process, once a protein is eaten on a given day, the dieter must continue to eat only protein, with absolutely no carbohydrates or fruit, for the remainder of that day.

In an article in the Nov. 15, 1981, issue of the *Journal of the American Medical Association*, Drs. Gabe B. Merkin and Ronald N. Shore wrote:

"Not only is there no scientific evidence to support this diet plan, but it also contradicts established knowledge about

Advice Aplenty But It's Really Simple Arithmetic

During the course of just about any year, a person contemplating going on a diet will have more than 100 magazine articles to peruse on the subject. Indeed, some magazines seem to reserve space in each issue for a weight loss article. For example, the entries under "diet" in a recent issue of the *Reader's Guide to Periodical Literature* had a listing that ran from the "At Work Diet" in *Mademoiselle* to "Your 10-day Midwinter Shape-up Plan" in *McCall's*.

Of course all that advice doesn't include other plans offered in the popular press, such as the *National Enquirer's* front page announcement of "Easiest Diet Ever." And it seems that there is always a place—usually near the top—on the non-fiction best seller list for a diet book.

With the woods so full of dubious diets, what is the best type of weight loss program to embark upon?

Nutritionist Marilyn Stephenson of FDA's Office for Nutrition and Food Sciences has evaluated many types of diets and has come to the following conclusion:

"If you follow just about any diet published in magazines or books you will lose weight. This is because these diets, regardless of whether they emphasize calorie counting, will fall in the range of 1,000 to 1,200 calories a day or less, and the ones that differ drastically from the usual way we eat force the dieter to change eating habits, which almost always result in a person's eating less.

"However, it is important in selecting a diet for weight loss, to be sure that you are not endangering your health. One of the best ways I know to do this is to go on a low calorie (1,000 to 1,200 a day) diet that is not extreme in either carbohydrate or protein intake and contains a variety of foods. This can often be done by simply eating smaller portions of the foods you ordinarily eat while minimizing the fat content."

Ms. Stephenson admits that for some people eating less of their usual fare involves more willpower than drastically changing the types of foods they eat. But although it may be harder, in the end it is safer and probably more productive in terms of changing eating habits. Stephenson also advises:

- Consulting a physician and then, if possible, a nutritionist or dietitian before beginning a diet. (It is particularly hazardous for people with specific diseases such as intestinal disorders, diabetes or disease to follow some types of diets.)
- Asking the physician if he or she would advise a vitamin and/or iron supplement, especially if the dieter is contemplating a diet under 1,200 calories.
- Keeping track of calorie intake with special attention to portion size.
- Eating several small meals a day instead of three larger ones.

Once a person is successful in losing weight, how can regaining it be avoided?

This question may have as many specific answers as there are persons who ask it, but in general, according to Stephenson, the most effective way to keep weight down is to continue the new eating habits developed during the weight loss diet while increasing calorie intake to a maintenance level.

For many Americans, this apparently means eating fewer than 1,500 calories a day according to data from the Health and Nutrition Examination Survey, 1971-75 (HANES-1). Reviewing this finding, Dr. Allan L. Forbes, FDA's associate director for nutrition and food sciences, notes that people consuming 1,500 calories a day need to pay particular attention to the amount of nutrients in the foods they eat. For example, green and yellow vegetables are a wise choice because they contain generous amounts of vitamin A and other nutrients but are low in calories.

"Most of the obesity in the U.S.," Forbes says, "results from a relatively tiny imbalance between daily energy intake and expenditure."

This means that only 50 to 100 extra calories daily, if consumed regularly, can add several pounds a year. Therefore, watching those small extra amounts of food will help avoid the unwanted pounds in the first place.

—J. Willis

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nutrition." They added: "Before a food can be absorbed into the bloodstream, it must be broken down by specific enzymes manufactured by the body. Enzymes in the food—the focus of Ms. Mazel's attention—are irrelevant to the absorption process. Food not broken down by enzymes will not be absorbed from the intestinal tract. It will pass out with the stool supplying no calories whatever. Contrary to the main contention of the Beverly Hills Diet, then, it is the *digested* food that has the potential to make you fat. Undigested food cannot possibly be fattening."

In their practices, these physicians have seen three patients on the Beverly Hills Diet with severe diarrhea, muscle weakness and dizziness, and they warn that the diet could result in a form of shock, low blood pressure and ultimately death, although there have been no reports of deaths of persons following the diet.

Dr. Mark Saginor, assistant clinical professor of medicine at UCLA, cautions that the diet has the potential to cause such side effects as diarrhea, gout, kidney stones, heart problems and strokes. Sami Hashim, nutrition professor at Columbia University, would add to these the risk of perforated peptic ulcers.

Diets come and diets go, and weight remains a problem for many in a country such as ours blessed as it is with relative prosperity and an ample food supply. But resorting to dangerous fad diets is obviously not the way to get better readings from the bathroom scale.

Judith Willis, editor of FDA's Drug Bulletin, *lost 35 pounds five years ago over a nine month period, eating 1,000 to 1,200 calories a day. She has not regained the lost weight, nor lost any more.*

On Getting The Lead Out Of Food

by Emil Corwin

"Tin cans" are somewhat misnamed. The metal is only 2 percent tin. The other 98 percent is steel. The tin is plated over the steel because tin is less subject to oxidation and resists acid. But while steel is sturdy and tin is relatively safe, there's another metal in most cans that's a problem. That metal is lead, which is used to solder some 20 billion cans of food each year. Lead seals up cans very well, but it's also toxic and some of it gets into the food supply.

Two-thirds of the lead found in canned foods comes from this solder, and this amount, in turn, constitutes one-third of the lead that the average person ingests from food. Other lead intake in humans comes from less easily controlled environmental sources, such as lead-based pesticides, automobile emissions, lead water pipes and paint chips.

Lead in food and drink has long been a concern of health professionals, government agencies such as the Food and Drug Administration and the canning industry. Through cooperative efforts between FDA and industry, the lead in canned foods has been reduced and continues to be reduced. This is the story of how it has been done.

Lead is one of the first metals known to mankind, and its toxic effects have been long recognized. Lead can cause anemia, as well as damage to the kidneys, the central nervous system in children, and to the peripheral nervous system in adults.

The method of preserving food in vessels of "tin" took hold in the United States around 1825. It was the brainchild of Thomas Kensett, called the "father of the canning industry in the United States." At first a hole was punched in the top through which chunks of fruit and vegetables were forced into the can. Lead solder was used to seal this vent hole as well as the side seam of the can.

The big advance in improving the can came at the turn of the century with the introduction of the "sanitary can." Instead of hand-soldering, the lid and bottom were mechanically crimped on and sealed with a rubber compound. Most important, solder was applied early to the side seam, which minimized its contact with food in the can.

The "sanitary can" (after the name of the manufacturer, the Sanitary Can Co.) increased production through rapid closing operations as well as elimination of the lead used to seal the vent hole and ends of the can.

The open-top, three-piece can came into wide use in the 1920s. In this period, the steel industry and canning manufacturers developed can linings of enamel and lacquer to prevent corrosion caused by fruit acids attacking the tin plate.

The yellowish or white enamel coating on the inside of some cans must comply with FDA food additive regulations. The coating is used for a number of food products including beer, carbonated soft drinks, some vegetables and seafood. It protects the contents from metal contamination, preserves their color and flavor and allows longer storage. "Coatings," says the Can Manufacturers Institute, "also prevent rust and corrosion, and in some cases, may reduce the cost of cans by permitting the use of less tin coating."

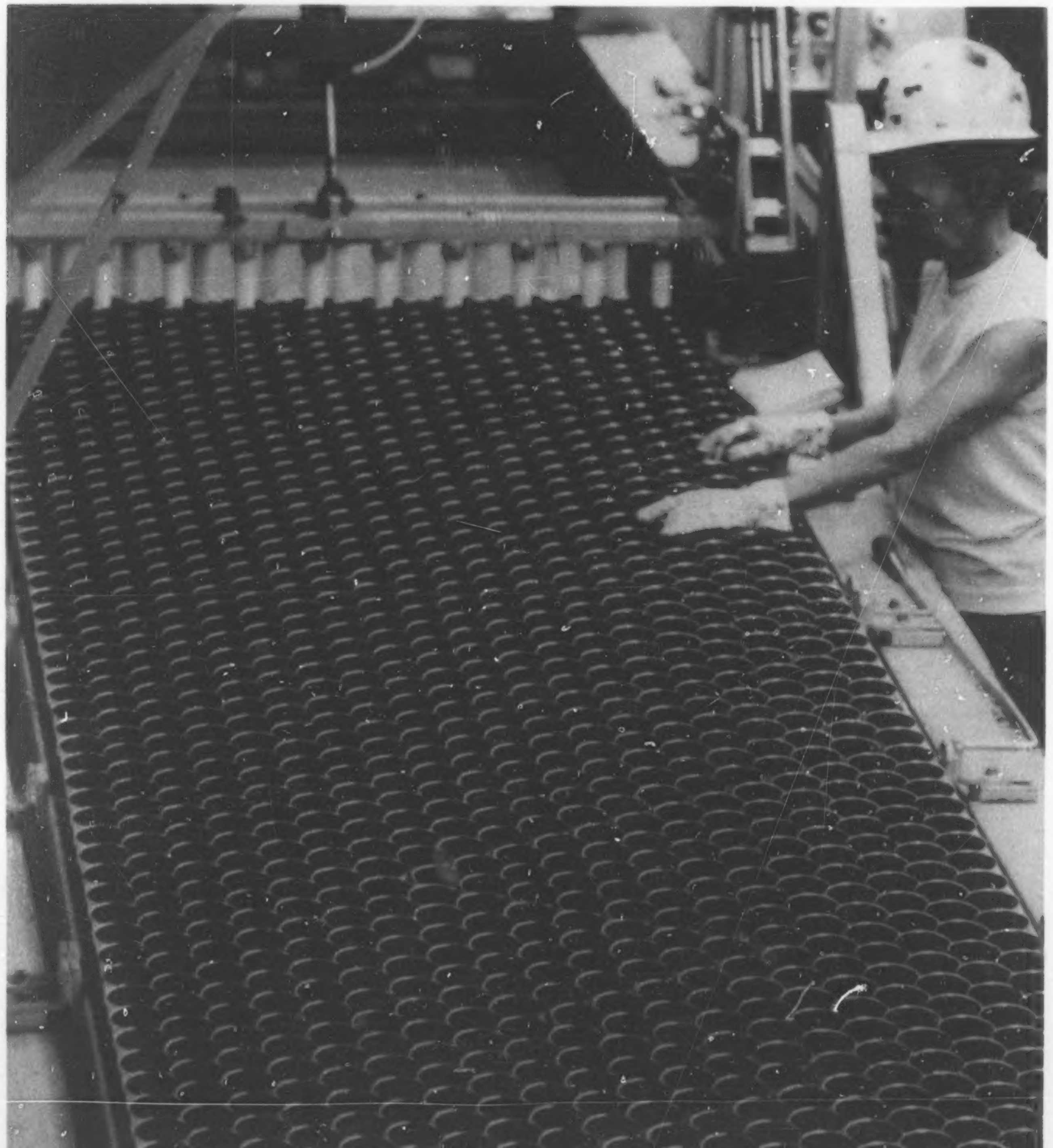
Probably more progress has been made in the past dozen years in reducing lead levels in food than in the 170 years since Nicolas Appert, a French chef, discovered the process of preserving foods in glass jars.

The very young are much more susceptible to lead exposure; they absorb approximately 40 to 50 percent of dietary lead as compared to 5 to 10 percent absorbed by adults. Because of this greater susceptibility, FDA has placed its main emphasis on the diets of infants and young children. Since recent studies have indicated that lead may cross the placental barrier and affect the developing fetus, FDA has also become concerned about the foods eaten by women of childbearing age.

FDA's program to reduce lead in food began in 1972 with evaporated milk, which at the time was widely used by mothers in preparing infant formula. Evaporated milk cans contained more lead than the conventional three-piece sanitary can, since its seams are traditionally soldered and the vent hole is closed with a solder plug after the can is filled through it. In 1973, the evaporated milk industry entered into a lead reduction program to ensure compliance with the FDA limit of 0.5 parts per million (ppm) lead in the product. As a result, the average lead level in evaporated milk declined from 0.52 ppm in 1972 to 0.08 ppm currently. That's an 85 percent decrease.

The use of evaporated milk has declined in the past 10 years, and now only around 1 percent of young infants consume formula prepared from evaporated milk, thus further reducing exposure to lead from this source. Most infant formula used today is ready mixed preparation in cans. The average lead levels in canned infant formula

Tin cans, such as those shown here at a can-making plant, are only 2 percent tin. They are named for the tin plate that is used over the can's principal material, steel. Lead is used to solder the seams of these cans and lead is toxic. However, industry and FDA have been working for years with considerable success to reduce the amount of lead that gets into food from the cans.



have been reduced from 0.10 ppm in 1974 to 0.02 ppm today, a decrease of 80 percent. Some of the reduction is because manufacturers have switched most of their production from lead-soldered cans to welded steel cans or seamless two-piece cans.

In another action, manufacturers of infant juices switched from cans to glass jars, resulting in reduction of average lead content from 0.30 ppm in 1973 to about 0.015 today, a 90 percent plus drop. Solid infant foods (fruits, vegetables and meats) have been packed for many years in glass jars; all evaporated milk and most infant formula are still packaged in metal cans.

The dramatic overall decline of average lead levels in infant foods is shown in the chart *(right)* in parts per million of lead.

Aside from evaporated milk, no "action level" has been established for these categories of food. An action level is the minimum amount of substance in a food at which the agency will take action to remove the food from the market—that is, seize the food or ask the manufacturer to recall it. In 1974, when the average lead level in evaporated milk was 0.52 ppm, FDA proposed a tolerance of 0.3 ppm, the lowest level it believed the industry could reasonably comply with at the time. Today, because of the industry's success in reducing lead content, FDA is considering setting even lower action levels than 0.3 ppm. Lead action levels are also being considered for food in other categories consumed by infants and young children to further reduce lead levels in their diets.

Results from FDA surveys of canned food for adults show that lead levels in the food have decreased somewhat in recent years. As an example, the average lead level of 13 popular canned adult foods analyzed by FDA in 1974 was 0.38 ppm. In a 1980 survey of about the same number of foods, the mean lead level had dropped to 0.21 ppm. The National Food Processors Association recently completed a study of over 500 samples of 24 typical canned products for adults, and reported an average lead content of 0.23 ppm, very similar to the FDA findings.

Types of foods	**1971-75**	**1976-77**	**1979-80**
Evaporated milk	**0.52**	**0.10**	**0.08**
Canned infant formula (concentrated)	**0.10**	**0.055**	**0.015**
Infant juices	**0.30**	**0.045**	**0.015**
Glass-packed solid infant foods	**0.15**	**0.05**	**0.03**

What about the future?

In August 1979, FDA announced that within five years it hoped to reduce lead in food from lead-soldered cans by at least 50 percent. With the progress in reducing lead in foods for infants, FDA has shifted emphasis to reducing lead in canned foods for adults that are also commonly eaten by infants and children.

Other changes under way to reduce or to eliminate lead in canned foods:

- An increasing number of canners are packing their foods in a seamless, two-piece can, a major innovation. It is estimated that packagers will be using the two-piece can at the rate of 4 billion containers a year by 1985.
- More cans are being made with electrically welded side seams, which eliminates the use of lead solder. The American Iron and Steel Institute believes the welded cans will eliminate soldered cans in the not-too-distant future.
- The manufacturers of infant formula expect by 1982 to be packing their products entirely in welded cans without solder or in seamless two-piece cans.
- The agency will continue to analyze samples of various foods annually for levels of lead as a way of assessing the effect of control measures instituted for canned food by the industry.
- In FDA's current survey, which will continue for at least three years, the agency is analyzing 10 canned foods for adults but also commonly eaten by children—tuna, apple juice, orange juice, string beans, baked beans, tomatoes, applesauce, chicken noodle soup, vegetable soup and fruit punch.

The advances that have been made in reducing lead in canned foods have been described as "one of the best success stories ever" by the industry and government working toward a common goal. The canners, the can makers and the FDA all are optimistic about meeting the goal the agency set in 1979 to reduce lead intake from food by half within five years.

Emil Corwin is a member of FDA's public affairs staff.

Some OTC Drugs That Work, Some That Don't

There was a little bit of good news and a lot of bad news in the latest round of panel reports coming out of FDA's review of ingredients in over-the-counter drugs.

The good news was that three ingredients—two for treating acute toxic ingestion (that is, accidental poisoning) and one for treating corns and calluses—were found to be safe and effective.

The bad news was that nothing is available that is good as digestive aids, deodorants for internal use, smoking deterrents, or for insect repellents for internal use or for oral treatment of fever blisters. It was recommended that hormones be eliminated from non-prescription skin, hair, scalp and other topically applied products, and mercury compounds were reported to be of dubious value in anti-microbials.

These were the conclusions of two of the 17 panels of experts established by FDA to review the safety and effectiveness of ingredients in all non-prescription drug products. By the end of this review, now in its 10th year, some 800 ingredients in 300,000 drug products will have been under scrutiny. The nine latest reports, published in the Jan. 5, 1982, *Federal Register*, bring to 45 the number of panel reports that have been issued for public comment. Still to come are 19 others.

Recommendations of the expert panels are not binding upon FDA. After the agency has evaluated the panels' reports and the public comments on them, monographs (i.e. standards) establishing the acceptable ingredients and labeling for the various products will be published.

Here is the essence of the nine panel reports, starting with the recommendations of the Advisory Review Panel on OTC Miscellaneous External Drug Products.

Corn and Callus Removers—The panel recommended that these products be used to treat calluses and hard corns only. Hard corns occur on the surfaces of the toe joints. Soft corns are whitish thickenings of the skin usually found on the webs between the fourth and fifth toes.

Salicylic acid is the only ingredient the panel found safe and effective for removing hard corns and calluses. They recommended it be used in concentrations of 12 to 40 percent in pads, plasters and discs, and at concentrations of 12 to 17.6 percent in a collodion base. Collodion is a solution of pyroxylin (nitrocellulose) in a solvent that leaves a transparent film when applied to the skin.

Phenoxyacetic acid and zinc chloride were considered safe by the panel but need additional testing to determine their effectiveness as callus and corn removers. There were no data demonstrating either safety or effectiveness for 13 other ingredients including glacial acetic acid, chlorobutanol, iodine, methyl salicylate and vitamin A.

Labels on the effective products can claim that they are "for the removal of hard corns and calluses," and should include warnings aginst use by diabetics or people with poor blood circulation. Labels should not include statements such as: "You are about to make your feet more comfortable," "Walk easy, walk soft" or "Dissolves corn or callus away."

KORRECT SHAPE.

Mercury-Containing Drug Products for Topical Anti-microbial Use—Mercury has been known to humans a long time and has been used in various ways for treating illness, the panel said, but it usually has been replaced by safer and more effective drugs. Science has shown that, as a class, mercury compounds are of dubious value for anti-microbial use, i.e., to treat bacterial infection. They act primarily by slowing the growth of bacteria. They can kill bacteria but this action is slow.

No mercury compounds were found by the panel to be safe and effective as topical anti-microbials and it recommended that seven mercury compounds be taken off the market. These are calomel, mercuric chloride, ammoniated mercury, merbromin, thimerosal, Ortho-hydroxyphenylmercuric chloride and phenylmercuric nitrate. Since mercury is not considered safe and effective, the panel said, no labeling would be recommended.

Topically Applied Hormone-Containing Drug Products—Estrogens and progesterone are sometimes ingredients in OTC drug products marketed for topical use as hormone creams and oils with the claim they will improve the appearance of skin and hair. However, the panel concluded that there is no evidence that using products containing hormones at a safe level will do any more good than using a cream alone. Such products cannot be considered safe and effective for their intended use.

Furthermore, the panel noted, hormones are often found in products sold as cosmetics. This leads the consumer into believing a more youthful appearance will result when in fact the changes that might occur cannot be seen with the naked eye, the panel said.

Six reports resulting from the deliberations of the Advisory Review Panel on Miscellaneous Internal Drug Products were included in the group published in January. Their recommendations:

Drug Products To Treat Acute Toxic Ingestion—An estimated two million accidental poisonings occur each year in the United States and about 60 percent of these involve children under 5. When a child swallows a toxic substance, the means to handle the situation should be available until medical help is obtained.

The panel said that two ingredients, activated charcoal and ipecac syrup, are effective for this purpose and further recommended that a kit containing both be developed.

Labeling for activated charcoal sold alone should include under "indications" the phrase "For the treatment of acute poisoning." Labels should also contain warning statements that a poison control center, emergency medical facility or physician should be called before the product is used; that the product should not be used in semiconscious or unconscious persons; and that if ipecac syrup has been used, the charcoal should not be administered until the patient has vomited.

Labeling for ipecac syrup alone should indicate that the product is for treatment of acute poisoning and should include a warning that the syrup not be used if the victim has swallowed strychnine, corrosives such as lye, and strong acids or petroleum distillates. Similar labeling would be required on acute toxic ingestion kits.

The panel also noted that no data are available on the safety and effectiveness of alcohol, magnesium hydroxide, potassium arsenite or tannic acid for the treatment of accidental poisoning. Thus, these ingredients should not be used in products intended to treat persons for toxic ingestion.

Smoking Deterrents—"Attempts by confirmed smokers to stop smoking are as numerous as are the different methods used," the panel said in this report. Unfortunately for those who need some help, the panel had nothing to offer. The group found no ingredients currently available that they considered safe and effective as smoking deterrents. Quinine ascorbate was considered safe but not effective as were a combination of licorice root extract, ground coriander, ground ginger, ground cloves, lemon oil and orange oil, and a combination of methyl salicylate, eucalyptus oil, menthol and thymol.

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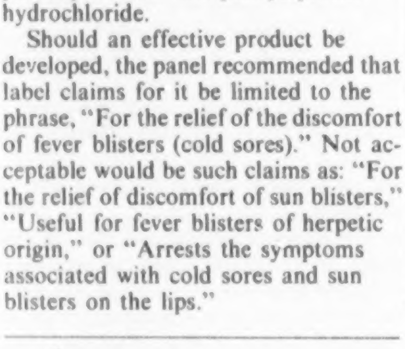
Recommended by the panel for further testing were lobeline and silver acetate. Lobeline is an alkaloid obtained from the herb *Lobelia inflata*. Silver acetate is a soluble silver salt. It leaves a nasty, sweet metallic taste in the mouth that makes smoking less desirable.

The panel recommended that, in the event an acceptable smoking deterrent becomes available, its labeling include a statement such as: "A temporary aid to those who want to stop smoking cigarettes," "Helps you stop the cigarette urge temporarily," or "A temporary aid to breaking the cigarette habit." The panel would also require this statement: "This product's effectiveness is directly related to the user's motivation to stop smoking cigarettes."

Drug Products for the Treatment of Fever Blisters—Fever blisters, or cold sores, are recurrent sores on the lips and other areas around the mouth, usually caused by herpes simplex virus. They are not to be confused with canker sores, which occur inside the mouth and may be associated with a variety of viruses, bacteria or fungi.

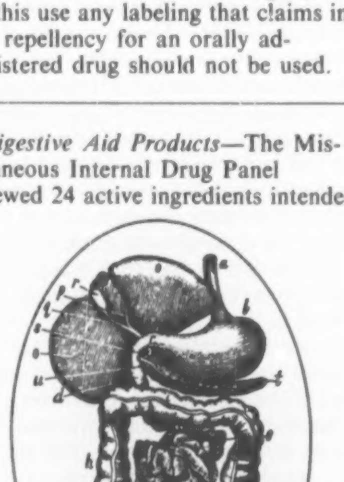
There are no ingredients in OTC drugs to be taken orally that are safe and effective in treating fever blisters, the panel said. However, three ingredients were found to be safe, although additional testing was recommended by the panel to establish their effectiveness. These are *Lactobacillus acidophilus* and *Lactobacillus bulgaricus*, which come from fermented milk cultures, and lysine hydrochloride. Five ingredients, not shown to be either safe or effective, should not be used in oral drugs for the treatment of fever blisters: acetaminophen, caffeine, chlorpheniramine maleate, phenolphthalein and phenylephrine hydrochloride.

Should an effective product be developed, the panel recommended that label claims for it be limited to the phrase, "For the relief of the discomfort of fever blisters (cold sores)." Not acceptable would be such claims as: "For the relief of discomfort of sun blisters," "Useful for fever blisters of herpetic origin," or "Arrests the symptoms associated with cold sores and sun blisters on the lips."



Oral Insect Repellents—For several decades scientists have tried to find a substance that could be taken internally to repel biting insects. In the United States these efforts have been directed almost entirely to mosquito repellents. Of the substances studied only thiamine hydrochloride (vitamin B_1) has shown enough promise to be evaluated to any extent. The panel on Miscellaneous Internal OTC Drugs concluded that although this ingredient is safe it is not effective as an oral insect repellent. And since there are no effective ingredients for this use any labeling that claims insect repellency for an orally administered drug should not be used.

Digestive Aid Products—The Miscellaneous Internal Drug Panel reviewed 24 active ingredients intended



to relieve the symptoms of either immediate post-prandial (after meal) upper abdominal distress or intestinal distress or both of these conditions. IPPUAD consists of sensations of bloating, distension, fullness or pressure with upper abdominal discomfort occurring within 30 minutes after a meal. Intestinal distress is abdominal discomfort occurring 30 minutes to several hours after a meal. Because this report was more extensive than the others in the group published in January it will be discussed in greater detail in a forthcoming story in *FDA Consumer* about the digestive system. It's enough to say here that none of the ingredients passed muster as being both safe and effective for these uses. Of the 19 ingredients intended to relieve post-prandial distress, nine were considered not effective and 10 were recommended for further testing. Of the 18 ingredients for intestinal distress, seven were safe but not effective and two were neither safe nor effective, while nine need further testing, according to the panel.

Deodorant Drug Products for Internal Use—Most body odors can be controlled by adequate personal hygiene. But there are some over which the individual has no control, such as the odors produced by an ostomy—any surgically-created opening for the external discharge of urine or feces—or by incontinence. The panel studied three ingredients intended as deodorants for internal use: bismuth subgallate, activated charcoal and water-soluble chlorophyllin. They found them generally safe for OTC use, but the data weren't sufficient to establish their effectiveness. Thus the panel called for additional testing.

The panel recommended that if any of these ingredients meet the test of effectiveness, labeling of products containing them include one or both of the following statements: "A colostomy or ileostomy deodorant," or "An aid to reduce odor from colostomies or ileostomies." The label should also state, "This product cannot be expected to be effective in the reduction of odor due to faulty personal hygiene." Activated charcoal products also should be labeled with the warning that the product may decrease the effectiveness of other drugs.

—Annabel Hecht

Pregnant Women Heed Advice

Advice to pregnant women flows in abundance. It comes from doctors, friends and relatives, and from books, magazines, newspapers, radio and television. All feed her interest and concern over how to bear a healthy child. In recent years, there has been a large volume of publicity—generated, in part, by the federal government—focusing on the potential dangers and hazards pregnant women and their unborn children face from the consumption or over-consumption of alcohol, caffeine, drugs in general and other substances.

But is the message getting across?

A recent report, based on a nationwide survey conducted for the Food and Drug Administration by the polling firm of Louis Harris and Associates, clearly indicates that it is, especially where the consumption of alcohol and caffeine-containing products is concerned. And, as might be expected, the highest level of awareness is among women 18 to 44, the child-bearing years.

However, even though those surveyed showed a high level of awareness to the potential dangers pregnant women face from consuming certain substances, their specific recall—that is, detailed knowledge—on the content of the warnings was not high. Some replied simply that a particular substance "harms the baby" and many others either could not recall the content of the warnings or they resorted to general answers.

More than 1,200 of the 1,499 respondents (80 percent) said they regarded the consumption of alcohol during pregnancy as a serious problem but only a third saw it as being serious enough to warrant direct federal action to deal with the problem. With caffeine, nearly 800 persons (53 percent) said caffeine consumption could be a serious problem during pregnancy but only 25 percent favored the idea of direct federal action.

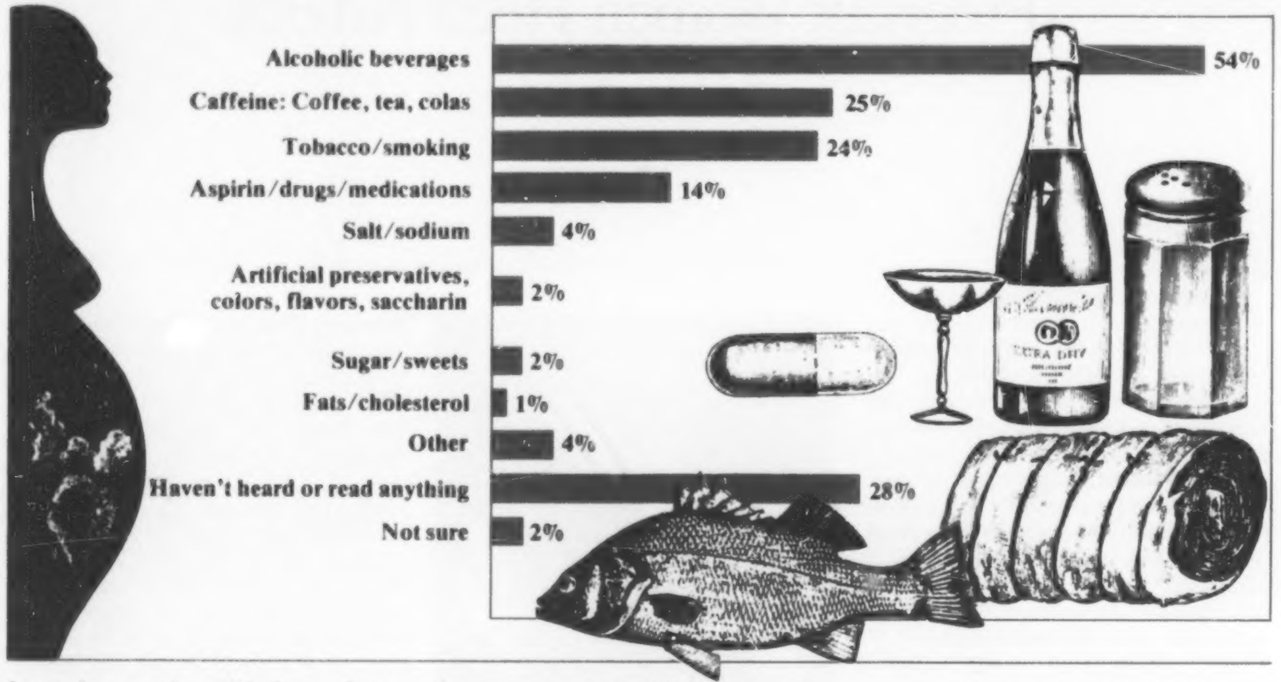
FDA's report, titled "Alcohol, Caffeine and Pregnancy: The Public View," was based on face-to-face interviews with those 1,499 people who were identified as the primary food shoppers for their households. The interviews were conducted between Dec. 1, 1980, and Jan. 12, 1981. Those interviewed included 242 men and 1,257 women, and among the latter were 593 women in the 18 to 44 age group. Also, a little over half of those participating were parents of at least one child. No attempt was made to determine if any of the participants were pregnant at the time or contemplated becoming pregnant.

The basic aim of the survey was to measure public awareness of the possible hazards pregnant women and their unborn children faced from consuming or over-consuming alcohol and caffeine-containing substances (coffee, tea, cola and pepper type drinks and other products), along with drugs in general and other substances.

The survey also sought to find out if the public knew specifically about the possible dangers of alcohol and caffeine consumption during pregnancy—issues that the Department of Health and Human Services and its affiliated agencies have emphasized more heavily in recent years.

Besides the public pronouncements of health officials, an example of the initiative taken at the federal level was the issuance of an instructive pamphlet titled "Alcohol and Your Unborn Baby." Prepared by the Alcohol, Drug Abuse and Mental Health Administration, the 14-page publication was first printed in 1978. Since then more than four million copies have been distributed. Citing the findings of recent scientific studies, the pamphlet provides a clear warning of the potential hazards from heavy drinking during pregnancy. It also expresses concern, based on some research data, that even low levels of alcohol consumption—two drinks a

"What have you recently read or heard of that pregnant women should not eat or drink, or eat or drink too much of?"



day, twice a week—might have adverse effects on an unborn child's development.

In 1980 FDA advised pregnant women to avoid or use sparingly foods and drugs containing caffeine. That advice was provided after an experiment conducted by the agency confirmed that caffeine, when fed to pregnant rats, caused birth defects and delayed skeletal development in the rat fetuses (*FDA Consumer*, Oct., 1980). The agency readily admitted that it didn't know how its findings might apply to humans, but officials thought that a warning, at least, was needed because of the widespread use of caffeine in coffee, tea, cola drinks, chocolate and many drugs. Further safety studies on caffeine were urged by FDA, and its educational efforts have focused on informing the public on caffeine-containing substances.

The educational campaigns at the federal level have also resulted in widespread publicity by the various news media. The basic approach used in the survey for FDA was to ask the shoppers whether they had read or heard about things that pregnant women should not eat or drink or consume too much of. The most significant answers were those obtained without any prompting—that is, where those interviewed freely recalled what they had read or heard. These answers fall into the category of "unaided recall." If those questioned could not freely recall anything, they were asked directly if they had read or heard anything about potential hazards associated with alcohol and caffeine consumption. The survey labeled those responses as "aided recall."

Overall, 70 percent of the 1,499 shoppers answered "yes" when asked if they had read or heard anything recently about substances that pregnant women should not eat or drink or consume in excess. More than half (54 percent) of the shoppers specifically mentioned alcohol and 25 percent recalled caffeine consumption. Another 24 percent also mentioned smoking and 14 percent were aware that pregnant women should be wary of their use of various drugs and medications, such as aspirin.

The percentages rose substantially when those who did not freely recall reading or hearing of the warnings were asked specifically about alcohol and caffeine. These are a less accurate barometer of public awareness since it is difficult to determine how much influence the prompting had on the answers.

Not surprisingly, women 18 to 44 years of age were more aware of the publicized warnings than were men and older women. Seventy-two percent of the 1,257 women interviewed for the survey and 77 percent of the 593 women in the 18 to 44 age group needed no prompting in replying that they had read and heard about the advice. Fifty-eight percent of the women in the main childbearing ages specifically mentioned hearing about alcohol and 34 percent about caffeine.

Is alcohol and caffeine consumption during pregnancy viewed as a serious problem? In the case of alcohol, 81 percent of those surveyed replied "yes." Fifty-three percent voiced the same view about caffeine. But the report clearly indicates that the public's perception of something being serious is not necessarily a call for direct federal action. Of the entire group of 1,499 persons, only 27 percent termed the alcohol problem serious enough to require federal involvement. In the case of caffeine, only 13 percent advocated federal action to deal with the issue.

The term "direct federal action" was posed to the respondents in a general way, the interviewers making no attempt to further define the term in talking to shoppers. Among those who did advocate a federal role, most suggested using the mass media or warning labels to better inform the public of the hazards to pregnant women.

Chris Lecos is on FDA's public affairs staff.

The Notebook

The Notebook: a potpourri of items of interest to consumers, gathered from FDA press releases, other news sources and the Federal Register *(designated FR with date of publication). The* Federal Register *is available in many large public libraries.*

■ FDA's Philadelphia Regional Office has opened a **new regional small business desk** to help firms obtain information and guidance about the requirements of laws administered by the agency. This is the fifth small business desk to be established by FDA since the program began in 1979.

■ To streamline government purchasing procedures, **FDA and the Department of Defense** have consolidated their medical products quality assurance programs. Under the agreement, made public Dec. 24, 1981, FDA will provide Defense with information about firms seeking to sell medical devices such as dental and surgical instruments, bandages and some X-ray equipment. FDA also may conduct inspections of firms and sample and test products offered for delivery. A similar agreement was signed in 1976 for drugs and biological products such as vaccines.

■ **F.D.& C. Yellow No. 6,** which has been used since 1929 to color foods such as gelatin desserts, sherbets, sodas, candies and cereals, as well as drug solutions, toothpastes and hair rinses, does not cause cancer, according to a carcinogenesis bioassay conducted by the National Cancer Institute. The report, "Bioassay of F.D. and C. Yellow No. 6 for Possible Carcinogenicity (T.R. 208)," is available from the Public Information Office, National Toxicology Program MD B-2-04, Box 12233, Research Triangle Park, N.C. 27709 (FR Dec. 11, 1981).

■ Chlorofluorocarbons are essential as lubricants for pharmaceutical rotary tablet press punches and thus are exempt from an Environmental Protection Agency rule prohibiting manufacture, processing and distribution of these **aerosol propellants**. The ban was imposed because of concerns that the fluorocarbons might destroy the protective ozone layer in the atmosphere (FR Jan. 5, 1982).

■ Vitamins are chemical nutrient substances necessary in very small amounts for life, growth and health. However excessive amounts do not have a vitamin function in the body, says the American Medical Association. Instead, the **vitamins act like drugs**. In a new publication, "Vitamin-Mineral Supplements and Their Correct Use," the medical group points out that individuals differ in their response to large amounts of vitamins and that poisoning from overdoses does occasionally happen.

■ To relieve the Freedom of Information office of an overwhelming paper burden, FDA has proposed changing the time of file retention. Except where denials and appeals are involved, the proposal would authorize disposal of FOI request files two years from the date of FDA's response to the request. This would mean an immediate **saving of $42,000** per year at current storage rates and would also allow the agency to keep, for longer periods, those files concerning FOI requests that were wholly or partially denied (FR Jan. 5, 1982).

■ U.S. school children have **fewer tooth cavities** today than they did in the last decade, Dr. Janet A. Brunelle of the National Institutes of Health told a meeting of the American Association for the Advancement of Science in January. A survey of 40,000 children aged 5 to 17, examined during the 1979-80 school year, showed the percentage of children without tooth cavities was 37 percent, up 9 percent from the early 1970s. Dr. Brunelle attributed the decrease to more community water fluoridation and increased use of fluoridated toothpastes. Changes in dietary habits also may have contributed to improved dental health, she said.

■ The Public Health Service is assessing what is known about the safety and effectiveness of single and multiple channel transcutaneous electrical stimulators for the **treatment of pain**. Anyone who wishes to submit information should write: Medical and Scientific Evaluation Staff, Office of Health Research, Statistics, and Technology, Room 17A-40, Parklawn Bldg., 5600 Fishers Lane, Rockville, Md. 20857 (FR Jan. 11, 1982).

■ FDA's food additive regulations have been amended to provide for the safe use of ethyl acetate as a solvent in the **decaffeination of coffee**. The rule, effective Jan. 5, 1982, is based on data contained in a petition filed by the General Foods Corp. (FR Jan. 5, 1982).

■ A proposal to bolster orange juice solids in frozen concentrated orange juice is being considered by FDA. Florida citrus groups petitioned FDA to amend the **standard of identity for frozen concentrated orange juice** to increase the minimum percentage of orange juice soluble solids from 11.8 percent to 12.3 percent when reconstituted according to directions. Petitioners want to establish a uniformly high level of soluble solids in frozen concentrate in all citrus producing areas. The Processors Council of the California-Arizona Citrus League says their oranges have greater consumer acceptability at the current level and that a higher level would mean the addition of more orange juice at higher cost to the consumer. Persons who wish to comment may write: Dockets Management Branch (HFA-305), FDA, 5600 Fishers Lane, Rockville, Md. 20857 (FR Jan. 8, 1982).

Investigators' Reports

Chelation Therapy Overdone

by John M. Couric

"There are none so credulous as sufferers from disease." So commented President William Howard Taft nearly 70 years ago about the willingness of the ill to believe medical claims even though unsupported by scientific evidence.

Today many sufferers from arteriosclerosis, hardening of the arteries, continue to confirm the keenness of the late president's observation. Some sufferers, faced with a sometimes painful and even fatal condition that surgery often can help, choose a procedure known as chelation therapy in which no surgery is involved.

This therapy, used on persons suffering from poisoning by heavy metals such as lead, is based on a chemical principle in which certain compounds or chelating agents are introduced into the bloodstream to form bonds with the metals. The compounds so formed then are excreted, ridding the body of the poisonous metals. FDA approves certain drugs for chelation treatment of this type of poisoning but does not approve them for treatment of arteriosclerosis. What's more, such a treatment can be dangerous and fatal.

The drug ethylenediamine tetraAcetate (EDTA or disodium edetate) has been illegally promoted by some persons for use in chelation therapy to treat arteriosclerosis. This treatment, promoted by a relatively small number of physicians, generally requires hospitalization for one or two weeks and is quite expensive. But some physicians advertise that the treatment can be given in their own offices.

Introduced into the patient's bloodstream through intravenous injection, an EDTA treatment can take up to four hours. Proponents claim that the EDTA surrounds the calcium deposits, or plaque, which clog the arteries. Supposedly, the deposits are then excreted through the urine.

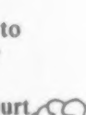
Unfortunately, EDTA is not one of those "if-it-won't-help-you-at-least-it-can't-hurt-you" drugs; in fact, it is far from benign. In ordinary use its principal harmful effect is kidney injury, which tends to occur when the daily dose exceeds 50 milligrams per kilogram of body weight. The effect can be fatal.

If EDTA or any other agent dissolves arteriosclerotic plaques abruptly, it would be anticipated that chunks of the calcium and fat-filled plaques would break off and lodge in a smaller blood vessel, blocking it. That's what can happen spontaneously in people who have arteriosclerosis and is a common cause of strokes. In at least one reported case, a patient under chelation therapy died when a calcium embolus, or clot, freed from a large arterial plaque lodged in his brain.

EDTA or disodium edetate is a useful drug in some patients who have severe hypercalcemia, a life-threatening condition caused by an excess of calcium in the blood. It also is used to treat some patients with heart function irregularities caused by poisoning from overdose or accidental ingestion of digitalis. However, FDA cannot permit claims by drug makers that disodium edetate is approved for treatment of hardening of the arteries. The agency first must have substantial evidence in the form of well-controlled clinical studies that the use of this drug in the chelation treatment for arteriosclerosis is both safe and effective. If a physician wishes to investigate the use of disodium edetate in the treatment of arteriosclerosis, he or she could do so by filing an application for an investigational new drug. No physician has.

Although a physician can use any drugs he or she wishes in treating a patient, the drug cannot be illegally labeled. In the case of prescription drugs, the term "labeling" includes advertising. That's why a federal court in Louisiana enjoined Dr. H. Ray Evers, and Meadowbrook Hospital, at Belle Chasse, La., from administering disodium edetate, calcium disodium edetate and other chelating agents to persons referred to the hospital for treatment of arteriosclerosis.

In granting the injunction the court noted that, "although several doctors



and a number of individuals testified . . . as to the beneficial effects of EDTA chelation therapy for arteriosclerosis," various other authorities testified that the therapy should be limited to cases of lead poisoning and even then there is a great risk. "The court in balancing the value of this testimony is satisfied that the possible benefits of the EDTA therapy . . . is far outweighed by the serious actual and potential damage caused by the drug in such therapy."

John M. Couric is a writer-editor in FDA's Bureau of Drugs.

Clammed Up

It was believed to be the stiffest penalty ever handed out for violations of Florida state shellfishing laws. Two men were sentenced to spend 45 weekends in jail, and a third, spared jail because of a lung condition, was fined $1,000. And that was only part of their punishment.

The three had been caught clamming on a portion of the Indian River in Florida that had been closed to shellfish harvesting by the **Florida Department of Natural Resources** because of a potential pollution hazard. They were clamming at night—another violation—and the court concluded, after hearing evidence, that they intended to sell the harvest to a seafood company for distribution to area restaurants.

In addition to receiving the jail sentence and fine, the shellfishermen were ordered to work one afternoon a week for the Salvation Army and to pay that organization $15 a week. Brevard County Judge Graham Stikelether also revoked the men's commercial shellfishing licenses for one year, except for two months during the summer when they will be allowed to "seed" (plant small seed oysters or clams) their leased areas under strict supervision of the Florida Marine Patrol. In addition, their boat was confiscated and they were ordered not to go on the Indian River for one year.

Said Judge Stikelether: "My primary concern was for public health. These guys had commercial clamming licenses; they knew they were clamming at night, which is a violation of the law; they knew they were going into an area that has been closed to clamming; and they were going to sell these potentially dangerous clams publicly."

Oysters and clams are filter feeders, which means they strain food from the water ingested into their systems. If the water is polluted, the pollution can concentrate in the shellfish in amounts potentially harmful to humans. Clams and oysters are frequently eaten raw or partially cooked, so it is important that shellfish be harvested only from clean, approved waters.

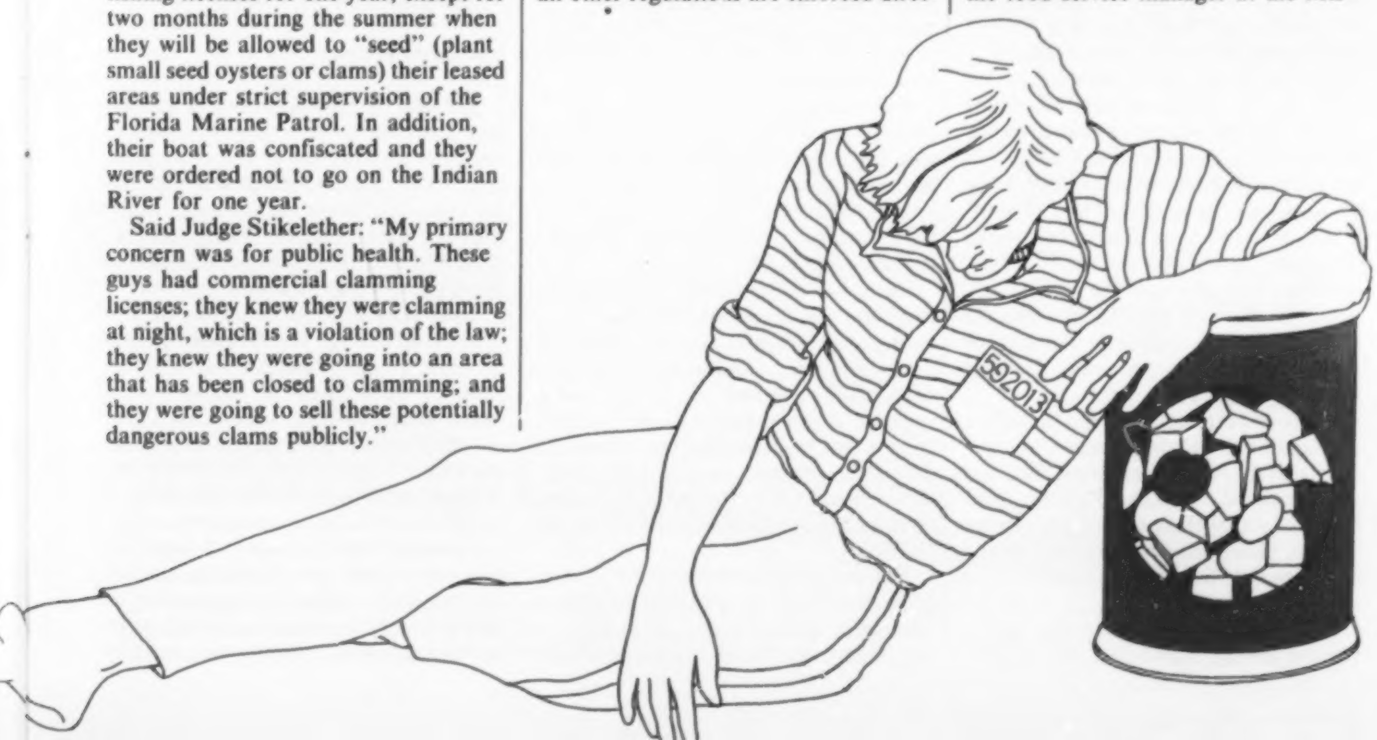
The part of the river where the three men were caught by the Florida Marine Patrol is near a shoreline that is being rapidly developed into condominiums, shopping centers and subdivisions. It was closed to shellfish harvesting by the Department of Natural Resources because the safety of the water could not be assured. One of many potential sources of contamination is discharge from a nearby waste water treatment plant. In addition, heavy rains wash polluting substances into the river, resulting in periodic closings of various sections of the river to shellfish harvesting.

In every shellfish-producing state, closings of harvest areas and virtually all other regulations are enforced directly by the states, even though the guidelines for their enforcement programs come from FDA's National Shellfish Sanitation Program (NSSP). FDA does not have the power to arrest violators such as the three men caught in Florida. Therefore, the states' enforcement powers are vital to the success of the NSSP. Each year FDA reviews all state shellfish sanitation programs. After reviewing Florida's program, FDA's regional shellfish sanitation specialist in Atlanta concurred with the state's decision to close portions of the Indian River to shellfish harvesting.

Suspects in Prison

An investigator in FDA's **St. Louis station** went to prison to investigate some suspects.

The suspects were swelled cans of fruit cocktail. The incident was unusual since the agency does not routinely inspect foods or drugs used in correctional facilities. The St. Louis station, however, was prompted to do so when the food service manager at the Mis-



souri Eastern Correctional Center in Pacific, Mo., called to complain that some cans of fruit cocktail had swelled.

When an FDA examination of the lot, stored in the prison commissary, confirmed the complaint, the distributor was notified so the parent lot could be examined. Meanwhile, prison samples were collected by the investigator for FDA laboratory analyses.

A visit to the distributor by FDA confirmed that cans from the parent lot also had swelled and the company agreed to initiate a recall of the product from its consignees. FDA's analyses revealed that the swelling was caused by hydrogen gas, which could indicate chemical decomposition in the cans. The company destroyed that lot, consisting of 1,315 cans and valued at $25,000.

The lot on hand at the prison was kept under embargo by the state until correction officials received permission to destroy it.

Checking on Blood

Many persons consider their blood a renewable resource with a definite market value, and a commercial blood industry has been built up around them.

At a commercial blood center a person can be paid $10 to $15 for surrendering a pint of blood, then come back in two months and give up another pint for another payment. If it is a plasmapheresis center rather than a whole blood operation, the plasma (fluid) will be extracted while the donor is there and the red cells returned to the donor in a saline solution. Plasma donors can be back within a week, since the body quickly replaces the lost fluid.

Whole blood is used for transfusions in surgery or accidents. Blood components are important in the making of human medicines. They include plasma derivatives, used as gamma globulin for immunizations and albumin for treating patients in shock.

There are almost 7,000 blood centers throughout the United States. Since 1975 they have been inspected, licensed and regulated by FDA to ensure that the conduct of their operations results in pure, safe and effective products and in safety for their donors, many of whom are regulars.

In a recent inspection of one such

vices in Charlotte, N.C., many deficiencies were found by FDA's **Atlanta district** office.

The center's staff did not take proper medical histories from donors and accepted some who were in obviously poor health. The center also accepted donors who had been permanently rejected (not allowed to give blood) because of prior exposure to hepatitis or venereal disease.

The center's staff used non-sterile cotton to clean the puncture site with alcohol, and whole blood was not stored at the proper temperatures.

The facility itself was badly maintained. It had bare wooden floors, exposed beams and loose plaster, and was generally unclean, with evidence of mice and roaches found in several locations.

FDA suspended the center's license to operate and to ship its products interstate. The center remained closed for two months while the facility and its operation were brought up to standard. FDA then made another inspection, found the violations had been corrected, and allowed Mid-South to resume operation.

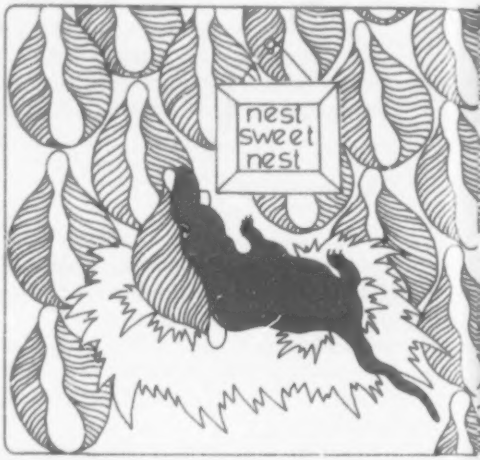
Corporate Responsibility

Not all companies wait for FDA to tell them when a product should be removed from the market. A recent instance was Merrell-Dow Pharmaceuticals, a Cincinnati firm that distributes Imferon Injection, an iron supplement made in England.

Imferon is an iron-dextrose compound intended for injection by persons with iron deficiencies who cannot take the supplement orally. It is administered in doses of 2, 5 and 10 milliliters, the level of dosage being extremely important.

Early in 1981, Merrell-Dow began receiving reports of muscle pain, stiffness and fever in patients taking the iron injections. A company review of each case found that the product itself was not at fault, but that the dosage level might be. Merrell-Dow concluded that some patients were getting larger doses than needed, and that some might be receiving Imferon who did not really require it.

The company decided on two courses of action, which it described to FDA's **Cincinnati district** office. It would



vials and ampules of Imferon already distributed to 15,000 outlets. It would then strengthen the warning label on the drug, stressing that a thorough diagnosis and laboratory tests should be done by the physician before Imferon Injection is prescribed. This would determine the individual's need for an iron supplement and establish the proper dose for that person. The label would also state that fatalities might occur if these precautions were not taken.

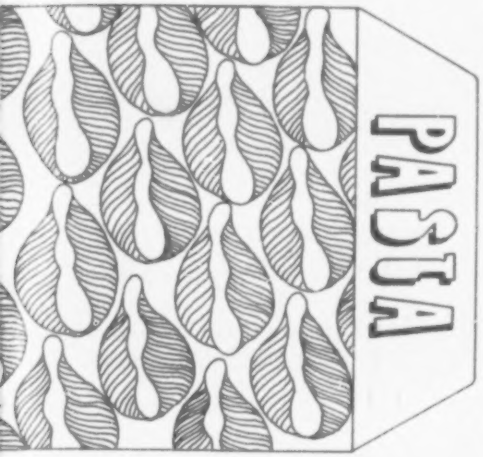
The drugs returned to the company—valued at $400,000—were destroyed. Future shipments of Imferon from the firm will carry the new warning label with its cautions on dosage.

Food for Hogs

The wad of paper and fuzzy material didn't belong there in the carton of pasta for a good reason: It was a rodent nest. There were nibble marks on packages of cheese and sausage, hundreds of dark pellets scattered on the floor and shelves, and dead rodents and insects in several locations.

Such was the state of affairs at a small food storage warehouse inspected by FDA's **Seattle district** last year. In samples taken by the investigator were rodent excreta pellets, insects and insect excreta. Several packages were rodent-gnawed.

Since adulteration and insanitary conditions were noted throughout the warehouse, FDA requested seizure of every food item that could be contaminated by insects or rodents. As a result, a U.S. marshal seized all food



metal or glass containers.

The firm, Pacific Food Importers of Seattle, then had the task of reconditioning—that is, separating the salvageable food from the unfit products to be disposed of. A sanitation consultant hired by the firm spent several weeks examining thousands of food containers for evidence of insect or rodent contamination. His efforts were checked by FDA. Adulterated food—valued at nearly $55,000—was converted to hog feed.

Pacific Food Importers also found it necessary to hire a pest control service to eliminate the vermin and make construction repairs to prevent more insects and rodents from entering the food storage area. Food in containers that could be penetrated by rodents or insects is now being stored at another facility.

Veal Un-drugged

A veterinarian in New Jersey who became, in effect, a manufacturer of animal drugs, has agreed to discontinue the line of unapproved antibiotics he had been supplying to farmers who raised calves for veal.

Dr. Robert R. Blease of Stewartsville, N.J., doing business as the Vet Med Co., had been manufacturing, packaging and distributing various injectable antibiotics to farmers in New Jersey and other states. Two of his products contained chloramphenicol, a compound that has not been proven safe for human consumption. FDA regula-

the animal tissue. Two other products contained penicillin which, if it remained in the veal, could cause an allergic reaction in persons sensitive to that drug. Blease also had included steroids in his products, and these too could affect some people who ate the veal.

FDA's **Newark district** investigators filed a complaint with the U.S. attorney for the District of New Jersey, asking that Vet Med be prohibited from introducing these unapproved animal drugs in interstate commerce. On Sept. 4, 1981, Blease entered into a consent decree of permanent injunction, agreeing not to "administer, prescribe or place in interstate commerce" such unapproved drugs for farm users with whom he does not have a valid veterinary practice relationship.

Inflated Claims

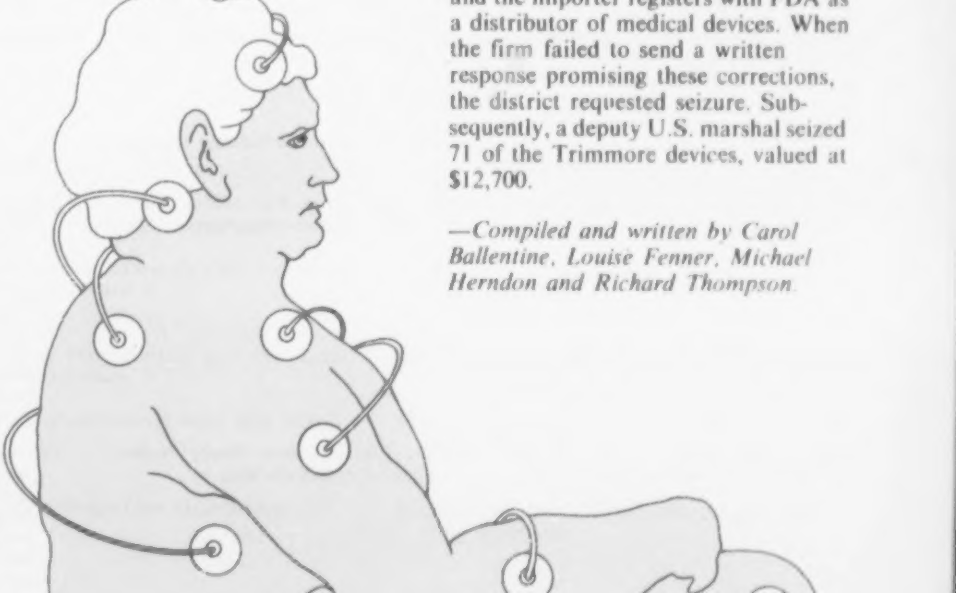
During a visit to a beauty trade show in New York City, the proprietor of a New Jersey skin and nail care salon became intrigued with the promotional literature attached to a certain device. Called the "Trimmore System," it was advertised primarily as a bust developer and consisted of sets of suction cups that were supposed to "stimulate the inner structure of the breasts . . . and develop a better bust-line."

But that wasn't the only way the device could be used, according to the labeling. Thumbing through the literature, the salon owner saw that the Trimmore supposedly could cure constipation, change body fat to energy, and relieve stress, stiffness and tension. In addition, the claim was made that the device would enhance the body's ability to "combat pollutants that fall on our cities," "wash out sulphur dioxide and cancer forming particles in the air we breathe," and "activate latent forces of life and health within us." The device, according to the labeling, was approved by FDA. The salon owner accordingly queried that agency about the product.

An investigator from the **New York district** was sent to collect a sample from the importer, RN International, Yaphank, N.Y. Close examination showed that the product, which had been imported from Japan, was suitable only as a mechanical massager. It would not affect the size of the breasts nor fulfill any of the other claims, and, of course, it had not been approved by FDA for anything.

The New York district sent a regulatory letter advising the importer that future shipments of the Trimmore would not be allowed into the United States until the mislabeling is corrected and the importer registers with FDA as a distributor of medical devices. When the firm failed to send a written response promising these corrections, the district requested seizure. Subsequently, a deputy U.S. marshal seized 71 of the Trimmore devices, valued at $12,700.

—Compiled and written by Carol Ballentine, Louise Fenner, Michael Herndon and Richard Thompson



Seizures and Postal Service Cases

FILED SEIZURE ACTIONS charge violations of the Federal Food, Drug, and Cosmetic Act and are initiated based upon FI mendations. A seizure action is commenced by the filing in the U.S. district court where the located. A U.S. marshal is then directed by the court to take possession of the goods, removing t from commerce, until the matter is resolved.

A total of 16 actions to remove from the consumer market products charged to be violative was reported in November. These actions included 12 involved charges concerning contamination, spoilage or insanitary handling; and 6 involved charges concerning economic and labeling violations. cluded 4 of drugs.

PRODUCT, DISTRICT & DATE FILED	FIRM & PLACE OF BUSINESS	CHARGES
	FOOD/Contamination. Spoilage. Insanitary Handling	
Blackeyed peas/U.S. District Court for the Eastern District of California 9/29/81	San Joaquin Crops Co. Inc./Wasco, Calif.	Product contains rodent and insect filth; held sanitary conditions.
Cherry pulp, frozen/U.S. District Court for the Northern District of New York 10/22/81	Clermont Fruit Packers Inc./Clermont, N.Y.	Product contains rotten cherries.
Cranberry sauce, jellied, canned/U.S. District Court for the Western District of New York 6/9/81	Manufactured from interstate components	Product is contained in rusted and leaking c
Flour mix for chapati/U.S. District Court for the Northern District of California 8/6/81	Bombay Bazar Wholesale Distributors/Berkeley, Calif.	Product contains insects; held under conditions.
Flour/U.S. District Court for the District of Puerto Rico 9/21/81	Borinquen Macaroni Corp./Yauco, Puerto Rico	Product held under insanitary conditions; co dent filth.
Flour/U.S. District Court for the Western District of New York 9/22/81	Barry Food Products Inc./Buffalo, N.Y.	Product held under insanitary conditions.
	FOOD/Economic and Labeling Violations	
"Honey" (two lots)/U.S. District Court for the Eastern District of Louisiana 12/10/81	Anthony's Syrup Co. and/or Oliver Anthony/Philadelphia, Miss.	Glucose and/or corn syrup have been subst honey; label of one lot is false and mis claiming that the product consists wholly and the label of the other lot is false and mi declaring the article to be honey but also ha of ingredients representing that the food part of corn sweetener and citric acid; lab the Fair Packaging and Labeling Act be quantity of contents statement was not ex fluid ounces followed in parentheses by a d of the largest whole unit.
"Honey"/U.S. District Court for the Eastern District of Arkansas 10/22/81	James Pilgrim and/or Sleepy Hollow Syrup Co./DeKalb, Miss.	Glucose syrup has been substituted for hone labeling is false and misleading in claimin to fact, that the food consists wholly of ho packed for Big Giant Foods, Oklahoma C product is not in compliance with the Fair and Labeling Act because the quantity o statement was not expressed in fluid ounce in parentheses by a declaration of the lar

PRODUCT, DISTRICT & DATE FILED	FIRM & PLACE OF BUSINESS	CHARGES
Protein supplement drinks, canned/U.S. District Court for the District of New Jersey 8/14/81	Universal Protein Supplements Corp./Linden, N.J.	Product had had saccharin substituted for sugar, the label lacked the common or usual name of each ingredient because saccharin was not declared; the label lacked the required hazard statement for products containing saccharin.
"Sesame" oil/U.S. District Court for the District of Hawaii 7/28/81	Taisei Trading Co., Ltd./Kobe, Japan	The valuable constituent, sesame oil, was omitted or abstracted from the product; soybean oil has been substituted for sesame oil; the product's labeling is false and misleading in representing the product as consisting wholly of sesame oil; and some lots fail to bear the nutrition labeling required by their vitamin claims.
"Sorghum" syrup/U.S. District Court for the Western District of Missouri 11/3/81	Griffin Manufacturing Co./Muskogee, Okla.	Glucose syrup substituted for sorghum; false and misleading labeling claiming article manufactured by Lemuel Roye Farms, Stigler, Okla., which was contrary to fact; false and misleading labeling claiming the article is made from sorghum cane; failure to conform to definition and standard of identity for sorghum syrup; and failure to comply with Fair Packaging and Labeling Act because the quantity of contents declaration was not separated from the printed label information appearing above and below the declaration, and was not expressed in a dual declaration of fluid measure.
"Sorghum" syrup/U.S. District Court for the Western District of Arkansas 9/18/81	Griffin Grocery Co./Muskogee, Okla.	Glucose syrup has been substituted for sorghum; the product's labels falsely and misleadingly claimed that the product consisted wholly of syrup from sorghum and that the product was manufactured by Lemuel Roye Farms, Stigler, Okla.; the product fails to conform to the definition and standard of identity for sorghum syrup; failure to comply with Fair Packaging and Labeling Act because the quantity of contents declaration was not separated from the printed label information appearing above and below the declaration; the quantity of contents declarations were in too small type size; and the quantity of contents statement of one of the two lots is not expressed in fluid ounces followed in parenthesis by a declaration of the largest whole unit of net quantity.
	DRUGS/Human Use	
Diethylpropion hydrochloride/U.S. District Court for the Northern District of California 8/6/81	Premo Pharmaceutical Labs. Inc./South Hackensack, N.J.	Product is a new drug without an effective approved New Drug Application.
Furosemide tablets/U.S. District Court for the District of Columbia 11/9/81	Premo Pharmaceutical Labs. Inc./South Hackensack, N.J.	Product is a new drug without an effective approved New Drug Application.
Furosemide tablets/U.S. District Court for the Central District of California 7/14/81	Superpharm Corp./Central Islip, N.Y.	Product is a new drug without an effective approved New Drug Application.
Estrone, estradiol & cyanocobalamin combination injection/U.S. District Court for the Eastern District of Missouri 11/16/81	Carter-Glogau Labs. Inc./Glendale, Ariz.	Product is a new drug without an effective approved New Drug Application.

U.S. POSTAL SERVICE

actions taken in medical cases as authorized in the Mail Fraud Statute (18 U.S.C. 1341) a
Representation Statute (39 U.S.C. 3005) as reported by the Chief Postal Inspector.

Complaints Filed by Law Department Under 39 U.S.C. (False Representation)

August 20, 1981: **James O. Anderson,** Waco, Ky. Advertising and sale through the mail of the product "An Herbal Treatment for Skin Cancer." The ad states, in part, "a medication that cleared her skin cancer. The simple remedy is given in the booklet to help any fellow human who is involved in this fight against the dreaded disease."

August 20, 1981: **Paul Andre, c/o Nancy Stone's Consumer Shopping Guide,** 5729 Pearl Rd., Cleveland, Ohio. Advertising and sale through the mail of the product "Hollywood Skinny Cream," representing the ability to cause weight loss. "At last, a positive cure! Proof that cellulite can be cured! Proof that you don't have to live with cellulite! This is the only technique we know of that will positively cure cellulite, and prevent its recurrence permanently."

August 25, 1981: **Herbal Concepts, Inc.,** 385 Bay Rd., Easton, Mass. Advertising and sale through the mail of the product "Au Naturel Cellulite Fighter." The ad states, in part, "the original cellulite fighter . . . if you've tried getting rid of cellulite using ordinary dieting methods or strenuous exercise, the original cellulite fighter is the easy alternative that works!"

August 25, 1981: **Elda Originals,** 180 N. Michigan Ave., Chicago, Ill. Advertising and sale through the mail of the prod
representing the ability to "lose unsightly fat in day
ling exercise or starvation diets . . . they exert gentle
which actually massages away layers of fat on your l
and bottom."

August 26, 1981: **Cosvetic Labs,** P.O. Box 1044, Deerfield B
tising and sale through the mail of the product "S
states, in part, "if you're feeling tired and run dow
just might be your 'endurance insurance'."

August 26, 1981: **Mega-Vital H.P.—Forte,** 340 W. Saint G
den, N.J. Advertising and sale through the mai
"Mega-Vital H.P. Forte with RNA." The ad stat
now possible to replenish or strengthen your body's
thereby helping the process of creating new, stron

August 28, 1981: **California Medical Research,** P.O. Box
Calif. Advertising and sale through the mail of th
Contour Creme," representing the ability to "Take o
and ugly inches without pills, shots, exercise or hu

False Representation Orders Issued by Judicial Officer Under 39 U.S.C. 3005

August 4, 1981: Against **Athena Products,** 3176 Marjan Dr., Atlanta, Ga. Satisfactory evidence was presented to the Postal Service that Athena Products, Ltd., and their representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Control," representing the ability to "curb appetites and promote fast weight loss."

August 10, 1981: Against **Cove Pharmacal Sales,** 95M South Hoffman Lane, Central Islip, N.Y. Satisfactory evidence was presented to the Postal Service that Cove Pharmacal Sales and their agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "PPA Plus Diet Capsules." The ad states, in part, "works so fast—the very first weekend alone you lose a full pound (of fluid and fat) every 8 hours! In fact—because you actually neutralize all the calories in the food you eat—you grow slimmer and slimmer from meal to meal . . . and stay slim for the rest of your life."

August 12, 1981: Against **R. J. Fitzgerald,** 521 Fifth Ave., New York, N.Y. Satisfactory evidence was presented to the Postal Service that R. J. Fitzgerald and their representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Sexy Slim #10." The ad states, in part, "one pill in the morning will quickly wash the fat down the drain. 10, 25, 50, 100 or more pounds easily safely . . . are you a round fat zero? Be a beloved sexy slim 10!"

August 31, 1981: Against **Standard Research Labs,** P.O. Box 9547, Ft. Lauderdale, Fla. Satisfactory evidence was presented to the Postal Service that Standard Research Labs and their agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Procaine Vitamin," representing the ability to "increase energy levels and stamina, as well as a greater sense of well being."

August 31, 1981: Against **Standard Research Labs,** P.O. Box 5009, Pompano Beach, Fla. Satisfactory evidence was presented to the Postal Service that Standard Research Labs and their representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Procaine Creme," an anti-aging treatment.

September 30, 1981: Against **Perry's Distributors,** 25 N. Beaver St., York, Pa. Satisfactory evidence was presented to the Postal Service that Perry's Distributors and their agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising "Stimulants." These stimulants are being sold as look-alike narcotics.

September 30, 1981: Against **R & K Sales,** P.O. Box 12589, Knoxville, Tenn.

device to obtain money by means of false represer
was advertising "Stimulants." These stimulants a
look-alike narcotics.

September 30, 1981: Against **Cosvetic Labs,** P.O. Box 14
Satisfactory evidence was presented to the Pos
Cosvetic Labs and their agents are engaged in condu
device to obtain money by means of false represer
was advertising the product "The South A
representing the ability to lose weight. "A painless
sheds pounds quickly and safely."

September 30, 1981: Against **Cosvetics,** P.O. Box 116
Satisfactory evidence was presented to the Pos
Cosvetics and their representatives are engaged
scheme or device to obtain money by means of fals
The firm was advertising the products "Digestaid
Eliminator," representing the ability to lose weigh

September 30, 1981: Against **Cosvetics,** P.O. Box 530
Satisfactory evidence was presented to the Pos
Cosvetics and their agents are engaged in conduct
device to obtain money by means of false represer
was advertising the products "Will Power" and "F
state, in part, "created expressly to reduce appetite"
make your body burn off your own fat."

September 30, 1981: Against **Cosvetics Labs,** P.O. Box 49
Satisfactory evidence was presented to the Pos
Cosvetic Labs and their representatives are engaged
scheme or device to obtain money by means of fals
The firm was advertising the product "1980
representing the ability to "help you achieve the slin
know you've always wanted."

September 30, 1981: Against **Braswell,** P.O. Box 116
Satisfactory evidence was presented to the Pos
Braswell and their agents are engaged in conduct
device to obtain money by means of false represer
was advertising the product "Guarana," representi
"eliminate hunger, causes euphoria, even while dietin
tal acumen and increases physical stamina."

September 30, 1981: Against **American Health Products,**
Atlanta, Ga. Satisfactory evidence was presented to
ice that American Health Products and their re
engaged in conducting a scheme or device to obtain
of false representation. The firm was advertis
"Formula—12 Creme." The ad states, in part, "her
to get rid of cellulite . . . if you want to get rid o

Notices of Judgment

NOTICES OF JUDGMENT on Seizure Actions

FOOD/Poisonous and Deleterious Substances

Shrimp, peeled and deveined, at New York, S. Dist. N.Y.

Charged 9-28-79: when shipped by Sunrise Foods Co., Kaohsing, Nationalist China, the article, labeled in part, "Early Dawn Peeled and Deveined — Individually Quick Frozen Shrimp . . . Packed For: AJC Intl. Atlanta, Ga., Product of Taiwan," contained the poisonous and deleterious substance salmonella micro-organisms, which might render it injurious to health—402(a)(1); and the article contained decomposed shrimp—402(a)(3). The article was claimed by AJC International Inc., Atlanta, Ga. A consent decree of condemnation authorized release to the claimant for export to the original foreign supplier. (F.D.C. No. 62449D; Import S. No. 216356; N.J. No. 1)

Spinach, bunches, Pleasant Valley, at Chicago, N. Dist. Ill.

Charged 11-4-81: when shipped by Pleasant Valley Vegetable Co-op, Oxnard, Calif., the article contained the non-conforming pesticide chemical monitor (methamidophos) and no tolerance or exemption from a tolerance had been granted for such pesticide chemical in or on spinach; 402(a)(2)(B). Consent decree ordered destruction. (F.D.C. No. 63593; S. No. 82-249-967; N.J. No. 2)

FOOD/Contamination, Decomposition and Insanitary Handling

Beans, kidney, black-eyed peas, and **pinto beans,** at Bronx, S. Dist. N.Y.

Charged 12-12-80: while held by Pelham Dairies Inc., Bronx, N.Y., the articles had been held under insanitary conditions; 402(a)(4). Default decree ordered destruction. (F.D.C. No. 62893; S. No. 81-138-215; N.J. No. 3)

Chocolate liquor, other cocoa product stocks, and **other food stocks,** at Philadelphia, E. Dist. Pa.

Charged 7-31-80: while held by Northern Shipping Co., Philadelphia, Pa., some of the articles contained mold and insect filth, and one lot of cocoa butter contained calcium hydroxide — 402(a)(3); all of the articles had been held under insanitary conditions — 402(a)(4); one lot of tea and two lots of cocoa beans lacked a label containing a quantity of contents statement — 403(e)(2); the labels of the tea, the cocoa beans and the cocoa butter lacked the name and place of business of the manufacturer, packer or distributor and lacked the common or usual name of the food — 403(e)(1); and the label of the chocolate liquor had mandatory information (i.e., name and place of business of the manufacturer, packer or distributor, the quantity of contents statement and the common or usual name of each ingredient) which was inconspicuous since such information did not appear on the label in the English language — 403(f). Consent decree authorized release of the articles to the dealer for salvaging. (F.D.C. No. 63109; S. No. 80-228-331; N.J. No. 4)

Cocoa press cake, sweet cocoa powder, and **cocoa cake,** at Hato Rey, Dist. Puerto Rico.

Charged 6-11-81: while held by Nutri Caribe Inc., Hato Rey, Puerto Rico, the articles contained insect filth and had been held under insanitary conditions; 402(a)(3) and (4). Consent decree authorized

Flour, and **other foodstocks,** at Brunswick, S. Dist. Ga.

Charged 2-28-81: while held by Glynn Distributors Inc., Brunswick, Ga., the articles were held under insanitary conditions; 402(a)(4). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63510; S. No. 81-289-169; N.J. No. 6)

Pecan logs, nut logs, and **milk-chocolate creamsticks (lemon, orange & coconut),** at Salt Lake City, Dist. Utah.

Charged 3-20-81: while held by Maxfield Candy Co., Salt Lake City, Utah, the articles had been prepared and packed under insanitary conditions; 402(a)(4). The articles were claimed by the manufacturer who denied that the articles were adulterated or that the articles had been introduced or held for sale after shipment in interstate commerce, and who asserted that the government had waived its rights and/or was estopped because of government assurance that the seized articles were not contaminated and were not injurious to health.

The government moved against hearing testimony about the absence of filth in a portion of the seized articles on the grounds of irrelevancy, since it is only necessary for the government to prove the existence of insanitary conditions that create a reasonable possibility of contamination. Subsequently, the claimant believed that the shelf life of the seized articles had expired. For the purposes of settlement of the action, the claimant consented to a decree ordering the articles destroyed. (F.D.C. No. 63415; S. No. 81-243-343 et al.; N.J. No. 7)

Rice, and **dog food,** at Statesboro, S. Dist. Ga.

Charged 10-1-81: while held by T. J. Morris Co., Statesboro, Ga., the rice contained rodent filth and both articles had been held under insanitary conditions; 402(a)(3) and (4). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63425; S. No. 81-239-129 et al.; N.J. No. 8)

FOOD/Economic and Labeling Violations

"Honey," Anthone's Wild Flower Brand, Anthone's "sorghum" syrup, and **Anthone's Ribbon "cane" syrup,** at Houston, S. Dist. Texas.

Charged 5-12-81: when shipped by Oliver Anthony, t/a Anthony's Syrup Co., Philadelphia, Miss., the articles had had glucose substituted for honey, sorghum syrup and cane syrup — 402(b)(2); the articles' labels were false and misleading in representing that the foods consisted wholly of honey, sorghum syrup or cane syrup — 403(a)(1); and the articles labeled "sorghum" syrup and "cane" syrup failed to conform to the respective definitions and standards of identity for sorghum syrup and cane syrup, since the articles were made with syrups derived from sources other than sorghum cane and sugarcane — 403(g)(1); and all of the articles except one lot of canned sorghum syrup were in violation of the Fair Packaging and Labeling Act because of failure to bear quantity of contents statements in prescribed terms—15 U.S.C. 1453(a)(3)(A)(i). Default decree ordered destruction by delivery to a charitable institution for use and not resale. (F.D.C. No. 63439; S. Nos. 81-260-910/3; N.J. No. 9)

"Maple" syrup, Pure Pioneer, at San Diego, S. Dist. Calif.

Charged 6-24-81: when shipped by Dewey Clark, Philadelphia, Miss., the article had had corn syrup substituted for maple syrup—

article failed to conform with the definition and standard of identity for maple syrup because the article was made with syrup from a source other than the maple tree — 403(g)(1). Default decree of condemnation ordered appropriate disposal. (F.D.C. No. 63444; S. No. 81-258-822 et al.; N.J. No. 10)

Protein supplement drinks, canned, at Linden, Dist. N.J.

Charged 8-14-81: while held by Universal Protein Supplements Corp., Linden, N.J., a powdered mix was blended, using interstate ingredients, which was subsequently manufactured into the liquid article and canned locally. The article, labeled in part, "Zero + 32 . . . A Nutritious 32 Gram Protein Drink . . . Strawberry [or 'Vanilla Malt,' or 'Chocolate' or 'Banana'] Manufactured for Universal Protein Supplements, Linden, N.J.," had had saccharin substituted for sugar — 402(b)(2); the label lacked the common or usual name of each ingredient because saccharin was not declared — 403(i)(2); and the label lacked the required hazard statement for products containing saccharin — 403(o)(1). Default decree ordered destruction. (F.D.C. No. 63518; S. Nos. 81-286-451/4; N.J. No. 11)

DRUGS/Human Use

Allopurinol tablets, at City of Commerce, C. Dist. Calif.

Charged 2-21-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). The article was claimed by the shipper. Pursuant to stipulation, the action was transferred to the District Court of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the article destroyed. (F.D.C. No. 62841D; S. No. 80-244-617 et al.; N.J. No. 12)

Allopurinol tablets, chlorthalidone tablets, diethylpropion HCl tablets, furosemide tablets, hydroxyzine pamoate capsules, spironolactone tablets, and **trimethoprim with sulfamethoxazole tablets,** at Tulsa, N. Dist. Okla.

Charged 1-28-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. A consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62760; S. No. 80-211-723; N.J. No. 13)

Allopurinol tablets, diethylpropion HCl tablets, and **furosemide tablets,** at Philadelphia, E. Dist. Pa.

Charged 3-6-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the District Court of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62805; S. No. 80-208-569; N.J. No. 14)

Allopurinol tablets, doxylamine succinate with B_6 tablets, and **prochlorperazine capsules,** at Valley Stream, E. Dist. N.Y.

Charged 4-25-79: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Consent decree ordered destruction. (F.D.C. No. 62258; S. No. 79-184-604; N.J. No. 15)

Amygdalin injectable and **amygdalin tablets,** at Buffalo Grove, N. Dist. Ill.

Charged 8-17-78: when shipped by M&R Electronics, Graham, Texas, the injectables, which were labeled in part, (vial) "Amygdalin CytoPharma 3g. 10 ml. CytoPharma De Mexico, SA.," and the tablets, which were in unlabeled plastic bags, had accompanying labeling (e.g., air bill listing the shipment as "Electronics" from M&R Electronics) which was false and misleading — 502(a); the articles' labeling lacked: (1) the name and place of business of the manufacturer, packer or distributor, and (2) lacked accurate quantity of contents statements — 502(b)(1) and (2); the labeling lacked the established name of the drugs — 502(e)(1)(A)(i); the labeling lacked adequate directions for use and was not exempted — 502(f)(1); the labels failed to bear the required prescription legend — 503(b)(4); and

Application — 505(a).

The articles were claimed by John E. Roche, M.
Ill., who denied knowledge concerning the misbra
denied that the articles were new drugs within the
U.S.C. 321(b), and claimed that under the April 8,
Rutherford v. *U.S.A.*, the claimant, as a physician fo
ill cancer patients with certain executed affidavits, wa
protection of that order.

At a hearing before the court, the claimant argued
fidavits had been provided and that the governmen
time to study them. The government argued that the a
appear to be in order and sought time for discovery

The government prepared written interrogatories f
claimant. Subsequently, the claimant withdrew his cla
Ultimately, a default decree of condemnation orde
destroyed. (F.D.C. No. 61890; S. Nos. 78-180-963/

Chlorpropamide tablets, at City of Industry, C. Dist. Calif.
Charged 6-13-80: when shipped by Pharmadyne La
Elmwood Park, N.J., the article was a new drug with
approved New Drug Application; 505(a). Default
destruction. (F.D.C. No. 63057; S. No. 80-245-421;

Chlorpropamide tablets, at Ft. Lauderdale, S. Dist. Fla.
Charged 6-5-80: when shipped by Darby Drug Co.
Centre, N.Y., the article, labeled in part, "Chlorpro
. . . Manufactured by Chelsea Laboratories, Inc., In
A Division of Rugby Laboratories, Inc.," was a new
effective approved New Drug Application; 505(a). De
dered destruction. (F.D.C. No. 62924; S. No. 80-19
18)

Chlorpropamide tablets, at New Britain, Dist. Conn.
Charged 12-28-78: when shipped by Premo Pharmac
tories Inc., South Hackensack, N.J., the article w
without an effective approved New Drug Applicati
shipper claimed the article, denied the charge and as
government was estopped, but admitted certain spec
government filed a motion for summary judgment o
and destruction asserting that all the requisite facts
admitted by Premo or previously decided adversely
court granted the government's motion for summar
ordered the article destroyed. (F.D.C. No. 61997; S.
N.J. No. 19)

Chlorpropamide tablets, at Port Washington, E. Dist. N.Y.
Charged 12-20-78: when shipped by Premo Pharmac
tories Inc., South Hackensack, N.J., the article w
without an effective approved New Drug Application;
ticle was claimed by the shipper who denied the char
that the government was estopped as a result of it
capricious action in the regulation of "new drugs."
consent decree of condemnation ordered the art
(F.D.C. No. 61999; S. No. 79-135-713; N.J. No. 2

Chlorthalidone tablets, at North Hollywood, C. Dist. Calif
Charged 2-13-80: when shipped by Pharmadyne La
Elmwood Park, N.J., the article was a new drug with
approved New Drug Application; 505(a). The article
the shipper. Pursuant to stipulation, the action was t
District Court of New Jersey for consolidation for tri
action. Subsequently, a consent decree of condemna
article destroyed. (F.D.C. No. 62819L; S. No. 80-2
21)

Chlorthalidone tablets, furosemide tablets, allopurin
trimethoprim with sulfamethoxazole tablets, at Br
N.Y.
Charged 2-29-80: when shipped by Pharmadyne La
Elmwood Park, N.J., the articles were new drugs wit
approved New Drug Application; 505(a). The artic
by the shipper. Subsequently, a consent decree of c
dered the articles destroyed. (F.D.C. No. 62833; S.

Chlorthalidone tablets, hydroxyzine HCl tablets, allopurinal tablets, furosemide tablets, hydroxyzine pamoate capsules, and **trimethoprim with sulfamethoxazole tablets,** at Ormond Beach, M. Dist. Fla.
Charged 2-12-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the District Court of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62802; S. No. 80-167-185 et al.; N.J. No. 23)

Diethylpropion HCl tablets, furosemide tablets, and **chlorothiazide with reserpine tablets,** at Brooklyn, E. Dist. N.Y.
Charged 3-28-79: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). Consent decree ordered destruction. (F.D.C. No. 62205; S. No. 79-161-324; N.J. No. 24)

Doxylamine succinate with B₆ tablets, at City of Commerce, C. Dist. Calif.
Charged 2-21-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). The article was claimed by the shipper. Pursuant to stipulation, the action was transferred to the District Court of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the article destroyed. (F.D.C. No. 62841E; S. No. 80-244-617 et al.; N.J. No. 25)

Furosemide tablets, at City of Commerce, C. Dist. Calif.
Charged 6-13-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (F.D.C. No. 63054; S. No. 80-245-421; N.J. No. 26)

Furosemide tablets, at North Hollywood, C. Dist. Calif.
Charged 2-13-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). The article was claimed by the shipper. Pursuant to stipulation, the action was transferred to the District Court of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the article destroyed. (F.D.C. No. 62819A; S. No. 80-208-582; N.J. No. 27)

Furosemide tablets, and **other specified drug stocks,** at Chicago, N. Dist. Ill.
Charged 2-29-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the District Court of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62842; S. No. 80-208-596 et al.; N.J. No 28)

Furosemide tablets, and **other specified drugs,** at Valley Stream, E. Dist. N.Y.
Charged 6-24-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the District Court of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 63010; S. No. 80-139-346 et al.; N.J. No. 29)

Furosemide tablets, chlorothiazide with reserpine tablets, and **diethylpropion HCl tablets,** at Hollywood, S. Dist. Fla.
Charged 3-27-79: when shipped by Pharmadyne Laboratories Inc., Hackensack, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the Eastern District Court of New York for trial with a similar action. Subsequently, a consent decree ordered the articles destroyed. (F.D.C. No. 62293; S. No. 79-166-559; N.J. No. 30)

Furosemide tablets, and **chlorthalidone tablets,** at Cleveland, N. Dist. Ohio.
Charged 2-4-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper who denied the charge. The government served written interrogatories on the claimant. Pursuant to stipulation, the action was transferred to the District Court of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62791; S. No. 80-208-554; N.J. No. 31)

Furosemide tablets, and **trimethoprim with sulfamethoxazole tablets,** at Philadelphia, E. Dist. Pa.
Charged 3-6-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the District Court of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62804; S. No. 80-208-568 et al.; N.J. No. 32)

Guaiacol combination injection, at Carolina, Dist. P.R.
Charged 1-29-81: when shipped by Carter-Glogau Laboratories Inc., Glendale, Ariz., the article, labeled in part, "Injection Guaiafage . . . guaiacol . . . cacodylic acid . . . beef peptone . . . propylene glycol . . . in water for injection . . . . Manufactured for: David Hurst, Inc., Hato Rey, Puerto Rico," was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (F.D.C. No. 63296; S. No. 81-274-502; N.J. No. 33)

Hydroxyzine HCl tablets, allopurinal tablets, chlorothiazide with reserpine tablets, diethylpropion HCl tablets, hydroxyzine pamoate capsules, and **spironolactone with hydrochlorothiazide tablets,** at Brooklyn, E. Dist. N.Y.
Charged 11-7-79: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62450; S. No. 79-162-182 et al.; N.J. No. 34)

Hydroxyzine HCl tablets, allopurinal tablets, diethylpropion HCl tablets, furosemide tablets, hydroxyzine pamoate capsules, and **trimethoprim with sulfamethoxazole tablets,** at Elmhurst, E. Dist. N.Y.
Charged 2-29-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without an effective approved New Drug Application; 505(a). The articles were claimed by the shipper. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62832; S. No. 80-208-588; N.J. No. 35)

Hydroxyzine HCl tablets, and **furosemide tablets,** at Orlando, M. Dist. Fla.
Charged 2-8-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the District Court of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered destruction. (F.D.C. No. 62803; S. No. 80-208-567; N.J. No. 36)

K.H.3 procaine HCl & hematoporphyrine capsules, three seizure actions, at Brownsville, S. Dist. Texas; Hidalgo, S. Dist. Texas; and Laredo, S. Dist. Texas.
Charged 5-2-80 and 5-5-80: when shipped by International Bonded Warehouses Inc., Laredo, Texas, the article, labeled in part, "K.H.3 Schwarzhaupt . . . zur Revitalisierung and Regeneration . . . Kapseln . . . Schwarzhaupt * Koln," was a new drug without an effective approved New Drug Application; 505(a). The article was claimed by the dealer who denied the charge. Subsequently, a consent decree of condemnation ordered the article destroyed. (F.D.C. No. 62938, 62935 and 62936; S. Nos. 80-192-974/5 and 80-122-314; N.J. No. 37)

Prochlorperazine capsules, at City of Commerce, C. Dist. Calif.
Charged 2-21-80: when shipped by Pharmadyne Laboratories Inc.

Elmwood Park, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the District Court of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the article destroyed. (F.D.C. No. 62841F; S. No. 80-244-617 et al.; N.J. No. 38)

Salicylamide, acetaminophen and antihistamine combination tablets, at Birmingham, N. Dist. Ala.

Charged 5-1-81: the article, which was labeled in part, "Soporific Tablets Non Prescription Sleep Aids" and which had been shipped by W. W. Sales Inc., Elkton, Md., was a new drug without an effective approved New Drug Application — 505(a); the article (whose tablets bore the embossed logo "Lemmon 714") was an imitation of another drug (Quaalude tablets) — 502(i)(2); and the article was a counterfeit drug, since without authorization the article bore the trade name, other identifying marks, imprint or likeness of a manufacturer other than the actual manufacturer, and thereby was falsely represented to be the product of such manufacturer — 201(g)(2). Default decree ordered destruction. (F.D.C. No. 63464; S. No. 81-163-643; N.J. No. 39)

DRUGS/Veterinary Use

Diethylstilbestrol (DES) implant pellets, at Omaha, Dist. Neb.

Charged 5-7-80: while held by Ronald L. Rosberg, Omaha, Neb., the article was a new animal drug and no approval of a New Animal Drug Application was in effect with respect to the article's use or intended use; 501(a)(5).

The article was claimed by Foxley & Co. (employer of Ronald L. Rosberg), Omaha, Neb., which denied the charge and served written interrogatories on the government. The government served requests for admissions and written interrogatories on the claimant. The claimant moved for a stay pending the outcome of another action involving diethylstilbestrol in the District of Columbia Circuit Court of Appeals. Subsequently, pursuant to stipulation the stay was lifted. The claimant moved for summary judgment and the government subsequently moved for summary judgment. The court granted the government summary judgment, saying:

"Pursuant to the warrant for arrest issued by this court, the above-captioned articles of drug were seized on May 16, 1980, by the U.S. marshal for this district. Foxley & Co. (hereinafter claimant) thereafter intervened in the action by filing a claim to the seized articles and an answer to the complaint. Based upon a stipulation by and between the United States and claimant, this court ordered that claimant be appointed custodian for the seized articles pending further court order.

"On the basis of the pleadings, answers to interrogatories, admissions on file and supporting affidavits, the parties have now cross-moved for summary judgment pursuant to Fed.R.Civ.P. 56. It is settled that summary judgment motions are appropriate in libel actions brought pursuant to the Act. *United States* v. *14 Cases, Etc., 'Naremco Medi-Matic,'* 374 F.Supp. 922, 926 (W.D.Mo. 1974); *United States* v. *Article of Device . . . Cameron Spitler*, 261 F.Supp. 243, 244 (D.Neb. 1966).

"In the brief in support of its motion for summary judgment, the United States essentially argues that: (1) there is no genuine issue as to the fact that the seized articles are new animal drugs which are unsafe and, therefore, adulterated within the meaning of the Federal Food, Drug, and Cosmetic Act; (2) the seized articles of drug are 'held for sale' by claimant as a matter of law since they are being held for a purpose other than the personal consumption of the ultimate consumer; and (3) whether the seized articles were legally adulterated when purchased and received by claimant is immaterial to this proceeding in view of the act's purpose to reach adulterated articles at all stages of commerce.

"In the brief in support of its motion for summary judgment, the claimant essentially argues as follows: (1) claimant's purchase of the seized articles, which occurred prior to the effective date of the decision by the FDA Commissioner to withdraw approval of New Animal Drug Applications for DES, was lawful; (2) the articles of drug containing DES purchased and received by claimant have not been 'held for sale' after October 31, 1979; (3) claimant is not in violation of the FDA's ban on the use of DES animal drugs since claimant has not implanted any cattle since the effective date of said ban (November 1, 1979); and (4) claimant's mere possession of the article of drug in question is not presently illegal.

"The chosen starting point for analysis of the above described cross motions for summary judgment is 21 U.S.C.A.§334(a)(1), which in pertinent part provides: 'Any article of food, drug, or cosmetic that is adulterated or misbranded . . . while held for sale (whether or not the first sale) after shipment in interstate commerce . . . shall be liable to be proceeded against while in interstate commerce, or at any time thereafter, on libel of information and condemned in any district court of the United States . . . within the jurisdiction of which the article is found . . . .'

"To obtain a judgment of condemnation of a seized article of drug under 21 U.S.C.A.§334(a)(1), therefore, the government must prove that the item seized is (1) a new animal drug (2) which is adulterated (3) while held for sale (4) after shipment in interstate commerce. The court now turns to a brief discussion of each of these requisite elements as applied to the case at bar.

New Animal Drug

"This court finds, and claimant does not contest, that the articles of drug containing DES, which were seized on May 16, 1980, constitute a new animal drug within the meaning of 21 U.S.C.A.§321(w). . . .

Adulteration

"A new animal drug is deemed to be adulterated [21 U.S.C.A.§351(a)(5)] for purposes of the act if it is unsafe [21 U.S.C.A.§360b(a)(1)(A)]. And such a drug is deemed to be unsafe unless there is in effect an approval of a New Animal Drug Application filed pursuant to 21 U.S.C.A.§360b(b) with respect to the use or intended use of such drug, or a notice of claimed investigational exemption under 21 U.S.C.A.§360b(j) is on file for the drug in question.

"The claimant, Foxley & Co., had admitted that there is no approved New Animal Drug Application in effect for the articles of drug seized in this action. . . . Further, claimant has filed no notice of claimed investigational exemption under 21 U.S.C.A.§360b(j) and Regulation 21 C.F.R.§511.1 (1980) with respect to the articles of drug in question. . . . As a result the court finds that the new animal drug seized herein is unsafe, and thus adulterated, within the meaning of the act.

Held for Sale

"Title 21, U.S.C.A.§334(a)(1) requires *inter alia* that adulterated articles sought to be condemned must have been 'held for sale' after their shipment in interstate commerce. Claimant apparently contends the United States has failed to demonstrate as a matter of law that the DES animal drugs in claimant's possession were held for sale at the time of seizure. In support thereof, claimant has submitted the affidavit of Jerald E. Swanson, D.V.M., an employee of Foxley Cattle Co. Dr. Swanson's affidavit states in part: 'The DES seized has not been held for resale by Foxley Cattle Co. nor implanted in any cattle owned by Foxley Cattle Co. after October 31, 1979 . . . .' Claimant has also represented that, at the time of seizure, the articles of drug containing DES were being held for return to their manufacturer in exchange for a refund of the purchase price. . . .

"It is well established that the terms 'while held for sale' as they appear in the Federal Food, Drug, and Cosmetic Act have been given by courts an expansive rather than a technical construction. *United States* v. *10 Cartons . . . Hoxsey Tablets*, 152 F.Supp. 360, 364-65 (W.D.Pa. 1957). Indeed, whenever there is a problem of construction involving the federal food and drug law, the duty of courts is to liberally construe provisions of the act, being mindful of its overriding purpose to protect the lives and health of the public. *Meserey* v. *United States*, 447 F.Supp. 548, 553 (D.Nev. 1977). In *United States* v. *Sullivan*, 332 U.S. 689, 696-97 (1948), the Supreme Court explained that the words 'while such article is held for sale after shipment in interstate commerce' apparently were intended by Congress 'to extend the act's coverage to every article that had gone through

"Courts have construed the 'held for sale' clause to cover situations in which adulterated or misbranded articles are held by a retailer, *United States* v. *Sullivan, supra*; a wholesaler, *DeFreese* v. *United States*, 270 F.2d 730, 731 (5th Cir. 1959), *cert. denied*, 362 U.S. 944 (1960); and a bailee, *United States* v. *Wiesenfeld Warehouse Co.*, 376 U.S. 86, 92 (1964). Physicians holding drugs for use in their practice may hold drugs for sale within the meaning of 21 U.S.C.A.§331(k). *United States* v. *Evers*, 643 F.2d 1043, 1050 (5th Cir. 1981). Devices, held by medical practitioners and used in the treatment of patients, are properly considered 'held for sale.' *United States* v. *Diapulse Corp. of America*, 514 F.2d 1097, 1098 (2d Cir.), *cert. denied*, 423 U.S. 838 (1975); *United States* v. *Article of Device . . . Cameron Spitler, supra*, 261 F.Supp. at 246. Owners of a bakery have been convicted of violating the act by holding adulterated flour for sale even though they planned to sell bread and rolls made from the flour rather than the flour itself. *United States* v. *Cassaro, Inc.*, 443 F.2d 153, 155 (1st Cir. 1971).

"This court subscribes to the view that an article of drug or device is 'held for sale' if it is used for any purpose other than personal consumption. *United States* v. *Articles of Device [Acuflex; Pro-Med]*, 426 F.Supp. 366, 368 n.3 (W.D.Pa. 1977); *see United States* v. *Article of Device . . . Cameron Spitler, supra*. The animal drugs containing DES at issue here clearly were not being held for personal consumption by an ultimate consumer, and were, therefore, 'held for sale' under 21 U.S.C.A.§334(a)(1). This conclusion is reinforced by the statement in Jerald E. Swanson's affidavit that, on December 20, 1979, claimant shipped 100,000 pellets of DES to Mexico, which shipment was subsequently returned to Foxley Cattle Co.

Shipment in Interstate Commerce

"As previously noted, 21 U.S.C.A.§334(a)(1) requires that the adulterated drugs sought to be condemned have been held for sale 'after shipment in interstate commerce.' Claimant herein admits that, prior to their seizure on May 16, 1980, the articles of animal drug in question had been shipped in interstate commerce. . . . Claimant asserts, however, that at the time it received the DES animal drugs, there was no legal restriction on their use, with the result that the nexus between the drug item and commerce, necessary to invoke federal jurisdiction, *United States* v. *Articles of Drug*, 585 F.2d 575, 585 (3d Cir. 1978), is not present in this case.

"Claimant's argument misses the mark. The language employed by Congress in 21 U.S.C.A.§§331(k) and 334(a)(1) broadly prohibits misbranding or adulterating articles held for sale after interstate shipment, without regard to, *inter alia*, how long after the shipment the misbranding/adulteration occurred or how many intrastate sales had intervened. *United States* v. *Sullivan, supra*, 332 U.S. at 696. 'Once an article is misbranded, it has violated the law and is subject to seizure at any time thereafter and no subsequent action can purge it from the violation.' *United States* v. *Article of Device . . . Cameron Spitler, supra*, 261 F.Supp. at 246; *see United States* v. *1,800.2625 Wine Gallons*, 121 F.Supp. 735, 738 (W.D.Mo. 1954). The above quoted principle applies to adulterated articles of drug as well as to misbranded articles of device.

"It has been admitted by claimant that the seized animal drugs are presently adulterated after shipment in interstate commerce. The fact that the seized articles may not have been legally adulterated before their shipment to, or receipt or use by, claimant is immaterial to the propriety of a judgment of condemnation under the act. The act was designed to safeguard the consumer from the time the article is introduced into the stream of interstate commerce all the way to the moment of delivery to the ultimate consumer. *United States* v. *Wiesenfeld, supra*, 376 U.S. at 92.

"In its brief in support of motion for summary judgment, claimant notes that this litigation arose after issuance of the FDA Commissioner's decision on withdrawal of approval of New Animal Drug Applications for DES, 44 *Fed.Reg.* 54852, which became effective June 29, 1979. Predicating its argument on the commissioner's decision, claimant states that the federal laws covering adulterated substances simply did not apply to DES animal drugs prior to June 29, 1979, and that it is not illegal to possess DES which was purchased prior to the effective date of the commissioner's determination.

"Claimant's argument is without merit. In plain, direct and unambiguous language, 21 U.S.C.A.§334(a)(1) provides that any adulterated article of drug which is held for sale after shipment in interstate commerce is subject to seizure and condemnation. Absent a clearly expressed legislative intention to the contrary, the language of a statute must ordinarily be regarded as conclusive. *Consumer Product Safety Comm'n* v. *GTE Sylvania, Inc.*, 447 U.S. 102, 108 (1980). Courts are not at liberty to modify by judicial construction the plain words of a statute or to depart from a statute's clear meaning under the guise of interpretation. *Adams* v. *Morton*, 581 F.2d 1314, 1320 (9th Cir. 1978); *Baker* v. *United States*, 460 F.2d 827, 831 (8th Cir. 1972). In situations where, as here, a statute's provisions are clear and unequivocal on their face, 'this court must follow the dictates of that statute.' *Sturdevant* v. *Wilber*, 464 F.Supp. 327, 332 (E.D.Wis. 1979).

"Considering that the articles of drug at issue in this action constitute a new animal drug that is adulterated while held for sale after shipment in interstate commerce, the court finds that there is herein no genuine dispute as to any material fact and that the United States is entitled to judgment as a matter of law." (F.D.C. No. 63002; S. No. 80-165-948; N.J. No. 40)

Nitrofurazone solution for dogs, cats and horses, at Long Beach, C. Dist. Calif.

Charged 11-9-79: when shipped by Vet Products Co., Kansas City, Mo., the article, labeled in part, "Glo-Vet . . . Nitrofurazone Solution . . . topical bacterial infections, genital tract infections and impaired fertility . . . Manufactured for Globe Veterinary Supply, Long Beach, California," was a new animal drug, and no approval of a New Animal Drug Application was in effect with respect to the article's use and intended use; 501(a)(5). The article was claimed by the shipper who denied the charge, denied that the article was a new drug and asserted that the action must be dismissed because the government had not developed an adequate administrative record to support a new drug determination. Subsequently, the government approved a New Animal Drug Application for Vet Laboratories (formerly Vet Products Co.) to produce nitrofurazone solution. Consequently, without admitting the government's charge, the claimant consented to a decree of condemnation and destruction. (F.D.C. No. 62672; S. No. 79-213-700; N.J. No. 41)

Medical Devices

Acu-Dot adhesive patch with magnet, at Huntington Beach, C. Dist. Calif.

Charged 11-30-79: the article, which was marketed by Acu-Dot Corp., Akron, Ohio, had labeling which contained false and misleading claims for the temporary relief of occasional minor aches and pains of muscles and joints; and the article's labeling lacked adequate directions for use for its intended purposes, since neither adequate direction for lay use nor adequate information for use by licensed practitioners could be provided; 502 (a) and (f) (1). The article was claimed by the marketing firm, which denied the charges and asserted a number of defenses. The government moved for summary judgment on the basis of *resjudicata* in a similar action in the Northern District of Ohio. The claimant did not dispute the prior adjudication, but asserted that the bond sought by the government for release for bringing into compliance was disproportionate. The court found in favor of the government, found that the article was misbranded, condemned the article, and authorized release of the article upon the filing of a bond in the amount of $300,000 or twice the value of the article if an appraisal showed the value to be less than $15,000; but, if no petition for other disposition was filed within 60 days, the marshal was to destroy the article. Utimately, the article was destroyed. (F.D.C. No. 62704; S. No. 80-214-153; N.J. No. 42)

X-ray system, Traceray IV, at Seattle, W. Dist. Wash.

Charged 10-16-79: the article, which had been manufactured by Western States Supply Ltd., Pueblo, Colo., was dangerous to health when used as directed because the device would emit radiation beyond false and misleading in claiming compliance with the regulation's standards, and in claiming that the device would deliver the radiation exposure stated in the instruction manual—502(a); and the article's quality fell below its purported quality—501(c). Consent decree authorized release to possessor for reconditioning. (F.D.C. No. 62558; S. No. 79-152-950; N.J. No. 43)

X-ray system, Traceray III, three seizure actions, at Morris, Dist. Minn., Coon Rapids, Dist. Minn. and Forest Lake, Dist. Minn.
Charged 10-15-79, 10-2-79 and 10-2-79: the articles, which had been manufactured by Western States Supply Ltd., Pueblo, Colo., were dangerous to health when used as directed because the articles would emit radiation beyond the pre-set exposure time—502(j); and the article's quality fell below its purported quality—501(c). Consent decree ordered destruction. (F.D.C. Nos. 62606, 62610, and 62611; S. Nos. 79-129-255, 79-129-257, and 79-202-845; N.J. No. 44)

Notices of Judgment on Criminal Actions

Cheek Wholesale Inc., William Cleo Cheek Sr., president, and **William Cleo Cheek Jr.,** vice-president & secretary-treasurer, at Atkins, E. Dist. Ark.
Charged 5-28-81: peanuts (count 1), roll mix (count 2), brownie mix, gingerbread mix, "goober" peanuts and sugar were held under insanitary conditions in a building accessible to rodents and insects; and the peanuts, roll mix, brownie mix, and gingerbread mix were contaminated with rodent or insect filth; 402(a)(3) and (4). Guilty plea by corporation; $1,000 fine on count 1, sentence suspended on other counts; probation for one year. Guilty plea by William Cleo Cheek Sr. to two counts; $500 fine on count 1; suspended sentence on other "goober" peanut count; and probation for one year. Guilty plea by William Cleo Cheek Jr. to two counts; $1,000 fine on count 2; suspended sentence on other sugar count; and probation for one year. (F.D.C. No. 63244; S. No. 79-137-524 et al.; N.J. No. 45)

Polar Bear Ice Co. Inc., t/a Alexandria Ice & Cold Storage Inc., and **Robert A. Moore,** president, at Alexandria, W. Dist. La.
Charged on or about 4-23-81: corn grits, whole wheat flour (two lots), macaroni and corn meal were held under insanitary conditions in a building accessible to rodents and were contaminated with rodent filth; 402(a)(3) and (4).

The defendants moved for a bill of particulars, moved for discovery and inspection of specified government evidence, moved to compel an election as to the various counts of the criminal information and for separate trials and moved to suppress inspectional and other evidence. The defendants also requested that the government serve notice of its intention to use any properly discoverable evidence. Subsequently, the corporation pleaded guilty and was fined $1,250. The individual pleaded guilty to the count involving corn grits; sentence was suspended and the individual was placed on probation for two years. (F.D.C. No. 63241; S. No. 79-171-779 et al.; N.J. No. 46)

Notices of Judgment on Injunction Actions

Briggs-Aitchison Co. Inc., and **Thomas Aitchison,** president, Wenatchee, E. Dist. Wash.
Charged 10-16-78 in a complaint for injunction: that the defendants processed, packed, held and distributed in interstate commerce brined cherries, which contained insect filth and which had been prepared, packed and held under insanitary conditions; that FDA inspections disclosed a number of specified insanitary conditions; that FDA analysis revealed the presence of insects on the cherries; and that the defendants had been repeatedly warned of the insanitary conditions and practices; 402(a)(3) and (4).

A consent decree of permanent injunction enjoined the complained of violations, and enjoined continued interstate operations unless and until a number of specified conditions had been met including the examination of all food on hand and the destruction or bringing into compliance of all contaminated food. Subsequently, the defendants

No. 78-148-672 et al.; N.J. No. 47)

Greer Laboratories Inc., William White Sr., president **William**
head of operations, and **Geraldine Douglas,** quality con
visor, Lenoir W. Dist. N. C.
Charged 10-24-78 in a complaint for injunction: that the
at their plant at Lenoir, N.C., had been engaged in: (a) m
ing, processing, packing, labeling and holding for sale, afte
shipment of components, certain articles which were
"Sterile Diluent for Allergenic Extracts" and as "Ste
Vials" which were intended as components of various dr
and (b) distributing such articles (drugs) in interstate com
the circumstances used for the manufacture, processing, p
holding of such drugs did not conform to and were not op
administered in conformity with current good manufact
tice; that FDA inspections of the defendants' plant reveale
of specified deficiencies; that FDA analyses of samples fou
samples contained particular matter indicative of inadequa
ing controls and testing; and that the defendants were well
their operations failed to conform with current good ma
practice; 501(a)(2)(B).

A consent decree of permanent injunction enjoined the
of violation and enjoined continued drug production unless
number of specified corrections were undertaken. (Inj. N
No. 78-100-869 et al.; N.J. No. 48)

Overisel Feed Supply Co., and **Adrian Slager,** president Hollan
Mich.
Charged 12-4-78 in a complaint for injunction: that the
manufactured, processed, packed, labeled and held variou
and non-medicated animal feed mixtures containing inte
ponents; that the circumstances used for the manufacturi
ing, packing and holding of the medicated animal feed mix
to conform with current good manufacturing practice;
medicated animal feeds differed in purity, quality and str
their purported purity, quality and strength due
contamination or sub-potency; that FDA analysis of
medicated feed showed sub-potency in chlortetracycline c
FDA analysis of bagged "non-medicated" animal fe
revealed contamination with 2.5 parts per million
famethazine, and FDA analysis of unbagged material (fro
chute after flushing) revealed 28 ppm sulfamethazine;
medicated animal feed mixtures contained non-confo
animal drugs; that non-medicated animal feed mixture
prepared, packed and held under insanitary conditions w
might have been rendered injurious to health; that FDA
disclosed a number of specified serious deviations from c
manufacturing practice; and that the defendants were well
their activities were in violation of the Federal Food,
Cosmetic Act; 501(a)(2)(B), 501(c), 402(a)(2)(D) and 40

The defendants opposed the government's action. How
hearing, the court granted a temporary restraining o
preliminary injunction enjoining the defendant, but per
manufacture of non-medicated feed provided that FDA h
that all equipment had been adequately cleaned. Over t
years, FDA inspected the firm's plant three times and
that the terms of the injunction were being met. Subseq
suant to stipulation of the parties, the action was dismiss
863; S. No. 78-121-217; N.J. No. 49)

Notices of Judgment on Miscellaneous Actions

Hearing aid device labeling, conditions for sale, and regulations p
by FDA, at Washington, D.C.
Charged 7-28-77 by American Speech & Hearing A
Rockville, Md., and Maurice H. Miller, Ph.D., Audiolog
hospital, New York, N.Y., against H.E.W. Secretary
Califano Jr., FDA Commissioner Donald Kennedy, and th
Drug Administration in a complaint for declaratory an

organization on its own behalf and on behalf of its approximately 3,500 member audiologists; that the ASHA and its member audiologists, including Maurice H. Miller, were adversely affected and aggrieved by proposed April 21, 1976, FDA regulations, entitled "Hearing Aid Devices: Professional and Patient Labeling and Conditions for Sale," because: (a) the regulations did not authorize evaluation by an audiologist as a condition of hearing aid sale, and (b) the regulations would pre-empt state laws which make evaluations by an audiologist a condition of hearing aid sales; that the FDA regulations required prospective hearing aid purchasers to have a medical examination by a licensed physician (but the medical examination could be waived by persons 18 or over except those demonstrating certain specified otological abnormalties) and the FDA regulations did not require hearing aid purchasers to obtain an audiological evaluation of their hearing loss (although numerous states had made an audiologist's evaluation a condition of hearing aid sales, either as a supplement or alternative to a physician's examination); that the regulations (as proposed by FDA) contained a "Non-Pre-emption Statement" which permitted state and local governments to establish more stringent conditions for sale of hearing aids than were prescribed by the FDA regulation; that FDA's final Feb. 15, 1977, rules retained the requirement of a medical examination and retained the right of waiver by any person 18 or over; including those demonstrating otological abnormalities, but, due to enactment of the Medical Device Amendments of 1976, the "Non-Pre-emption Statement" was nullified so that the final rules were the opposite of the proposed rules in that state and local legislation relating to hearing aids was pre-empted; that FDA's action in limiting the phrase "practitioner licensed by law to administer or use such device" to mean "physician" and to exclude licensed audiologists was arbitrary, capricious, an abuse of discretion and otherwise not in accordance with law. FDA's inclusion of the "Non-Pre-emption Statement" in the proposed rules despite the pendency of the Medical Device Amendments misled and deceived readers into believing that the rules would not pre-empt state and local legislation requiring examinations by audiologists; that the termination of the comment period for the proposed rules, prior to the adoption or even proposal of regulations on exemption from pre-emption, deprived the plaintiffs of a fair opportunity to comment on the proposed rules for hearing aids; and that the court should declare invalid FDA's final rules, enjoin the taking effect of the rules, require a new rule making proceeding, and declare invalid FDA's interpretation of the word "practitioner."

The Hearing Industries Association, a national trade association of firms engaged in the manufacture, import and distribution of hearing aids, moved for leave to intervene in the action to protect the interests of HIA and its member firms. The motion of HIA to intervene was granted.

The court denied ASHA's motion for a preliminary injunction, saying:

"In this suit for declaratory and injunctive relief the American Speech and Hearing Association, a national association of audiologistis and speech pathologists, and Maurice H. Miller, a member of ASHA, seek to prevent the Food and Drug Administration from implementing final rules governing the manufacture and distribution of hearing aid devices. The rules were due to become effective on August 15, 1977. Briefs were filed on an expedited schedule, and a hearing was held on August 12, 1977, at which time the court granted leave to intervene as a defendant to the Hearing Industries Association.

"The sequence of events precipitating this lawsuit is straightforward. Presently, the marketing of hearing aid devices is regulated, if at all, by the states. Forty-one states have such rules, but their provisions vary widely. For example, in some states that regulate the devices, an examination by a specialist physician or an audiologist or both is required as a condition precedent to obtaining a hearing aid; some states require no examination at all. Rules in some states apply only to certain age segments of the population.

"In March 1974 the defendant, Department of Health, Education, Comments were solicited, public hearings held and a report prepared. As a result of the task force findings, and acting pursuant to its authority under 21 U.S.C.§371(a) (1970) and 21 C.F.R.§2.120(a)(1) (1976), the FDA undertook to develop national rules. Proposed rules were published in the *Federal Register* on April 21, 1976, and a 60 day comment period was provided. 41 *Fed. Reg.* 16756 (1976).

"Section 801.421(a) of the proposed rules required an examination, subject to waiver in certain instances, by a licensed physician prior to issuance of a hearing aid to a user. It also provided that '[s]tate and local governments may make more stringent conditions for sale of hearing aids.' Thus, those state rules requiring an examination by an audiologist in addition to one by a physician were left intact.

"On May 28, 1977, however, during the comment period for the proposed rules, Congress passed the Medical Device Amendments of 1976, Pub. L. No. 94-295,[1977] *U.S. Code Cong. & Ad. News* (90 Stat. 539). The amendments mandate pre-emption of state and local requirements with respect to medical devices (including hearing aids) which are 'different from, or in addition to' any requirements established by the FDA. 21 U.S.C.A.§360k(a) (West 1977 Supp.). However, the amendments do allow the FDA, by regulation issued after notice and an opportunity for an oral hearing, to exempt a state or local medical device requirement from pre-emption under such conditions as the FDA may prescribe if the requirement is (1) more stringent than the federal requirements applicable to the device or (2) required by compelling local conditions and compliance with it would not cause the device to be in violation of any other federal requirement. *Id.* §360k(b). On June 4, 1976, the FDA published in the *Federal Register* a notice of the new amendments, 41 *Fed. Reg.* 22620 (1976). However, no mention was made of either the effect of the amendments on the proposed hearing aid rules or the FDA's intention to issue any regulations governing exceptions.

"The hearing aid rules were promulgated in final form on February 15, 1977, to become effective on Aug. 15, 1977. 42 *Fed. Reg.* 9286 (1977). The requirement of prior examination by a *physician* was retained, but, due to the intervening enactment of the Medical Device Amendments, providing pre-emption, no allowance was made for differing state and local regulations.

"Plaintiff ASHA filed petitions for stay and for reconsideration of the final rules with the FDA on March 17, 1977, thus exhausting its administrative remedies. The petitions were denied June 14, 1977, and on the same day the FDA issued proposed rules for exemption of state medical device requirements. *Id.* at 30380. Final exemption rules have not yet been promulgated.

"Plaintiffs' legal claim is two fold. First, plaintiffs object to use of the word 'physician' in the final rule requiring a written statement by a physician as a condition precedent to the purchase of a hearing aid. The rule was promulgated pursuant to 21 U.S.C.A.§360j(e)(1)(A)(West 1977 Supp.), which provides: 'The Secretary may by regulation require that a device be restricted to sale, distribution, or use . . . . only upon the written or oral authorization of a *practitioner* licensed by law to administer or use such a device. . . . (emphasis supplied).' Plaintiffs contend that in several states audiologists are 'practitioner[s] licensed by law to administer or use' a hearing aid. Therefore, it is argued, use of a term more restrictive than 'practitioner' in the regulation is arbitrary and in contravention of the statute. The extent to which this semantic shift affects plaintiffs is unclear from the present record; evidence on the functions and employment of audiologist was insufficent and contradictory.

"Plaintiffs also challenge the procedure followed in promulgating the final hearing aid rules. Defendants are charged with failure to give notice of the 'drastic alteration' of the proposed rules by pre-emption provision of the amendments, with not affording sufficient time after passage of the amendments for comment on the proposed regulations, and with delaying publication of proposed medical device exemption rules until after issuance of the final hearing aid regulations. Plaintiffs allege that these actions violated the notice and comment provision of the Administrative Procedure Act, 5 U.S.C.§553 (1970), . . . thus depriving them of an opportunity for meaningful participation in the formulation of the final rule. In opposition, defendants deny that any of the amendments, had actual notice of the new law and therefore could not have been prejudiced by the FDA's inaction. Defendants represented to the court that pending implementation of final exemption rules the FDA is actively considering individual state exemption requests on an ad hoc basis.

"There is no question that plaintiffs have raised serious legal questions as to the propriety of the FDA's actions. However, this alone does not warrant interim injunctive relief. Something more must appear. 'An order maintaining the status quo is appropriate when a serious legal question is presented, when little if any harm will befall other interested persons or the public, and when denial of the order would inflict irreparable injury on the movant.' *Washington Metropolitan Area Transit Commission* v. *Holiday Tours*, slip op. at 6, C.A. No. 76-1500 (D.C. July 5, 1977), *interpreting Virginia Petroleum Jobbers Ass'n* v. *FPC*, 259 F.2d 921 (D.C. Cir. 1958).

"The plaintiffs' showing of irreparable injury was inadequate. When questioned by the court, plaintiffs pointed to the 'confusion' that would accompany implementation of the rules and the loss of business that audiologists might suffer. The first claim is frivolous; the second is not persuasive. While the court does not hold that economic injury can never constitute sufficiently irreparable injury to warrant injunctive relief, *cf. Independent Bankers' Ass'n* v. *Smith*, 534 F.2d 921, 950 (D.C. Cir. 1976), *cert. denied*, 45 U.S.L.W. 3253 (1977), the plaintiff must come forward with something more than a conclusory allegation. Counsel could not, at this stage of the proceedings, establish what portion of plaintiffs' business would be adversely affected by the rules, or why the injury would be irreparable if the rules became effective. Perhaps such a showing will be made in a hearing on the merits after appropriate discovery, but on the present record there is insufficient evidence to establish the irreparable injury that would warrant the granting of preliminary relief."

The plaintiffs appealed the denial of a preliminary injunction and moved for a stay of the effective date of the final rules. The Court of Appeals denied the motion because it appeared that FDA was currently considering requests for exemption from pre-emption on an *ad hoc* basis, and that consequently the denial of a stay would not adversely affect local governments.

As to ASHA's still pending request for a permanent injunction, the government and the other defendants moved to dismiss on the grounds that ASHA had failed to state a claim upon which relief could be granted. HIA joined in the defendants' motion; and the plaintiffs countered with their own motion for summary judgment. After a hearing before the court, the court took the case under advisement. HIA, the intervenor, filed a synopsis to the document in question and included, as attachment 1, a letter of Nov. 22, 1977, from the intervenor's counsel. Upon motion of ASHA, the court struck such letter from the record.

In ruling on cross motions of summary judgment, the court upheld the FDA and granted summary judgment against ASHA, saying:

After the rules became effective, defendants filed a motion to dismiss under Rule 12 (b)(6) of the Federal Rules of Civil Procedure. The Hearing Industries Association, an intervenor-defendant, joined in this motion. Plaintiffs countered with a motion for summary judgment. All motions have been duly opposed, and the oppositions replied thereto. At the conclusion of an exhaustive oral argument, the court invited the parties to submit supplementary papers on the role of the audiologist in the hearing aid delivery system. Only HIA chose to submit. The case is now ready for decision. After careful consideration of the entire record, and treating defendants' motion as one under Rule 56 of the Federal Rules of Civil Procedure, the court grants summary judgment to defendants, and denies it to plaintiffs, in all respects.

I.

"The material facts are not in dispute. Prior to implementation of the challenged regulations, the marketing of hearing aid devices was regulated, if at all, by the states. Abuses were prevalent. Although 43 states had rules governing some aspect of hearing aids, the provisions varied widely in both force and scope. In some states an examination by a physician specializing in hearing disorders or an audiologist was required as a condition precedent to obtaining a hearing aid. Som states required no examination at all. Rules in some states applic only to certain age segments of the population.

"In March 1974 the defendant, Department of Health, Educatio and Welfare, established a task force to study problems relating to t marketing of quality hearing aids throughout the United State Comments were solicited, public hearings held, and a report prepare As a result of the task force findings, and acting pursuant to i delegated authority under 21 U.S.C.§271(a) (1970) and 2 C.F.R.§21.120(a)(1) (1976), the FDA undertook to develop nation rules. Proposed rules were published in the *Federal Register* on Ap 21, 1976, and a 60 day comment period was provided. 41 *Fed. Re* 16756 (1976).

"Section 801.421(a) of the proposed rules required an examinatio subject to waiver in certain instances, by a licensed physician prior t issuance of a hearing aid to a user. It also provided that '[s]tate ar local governments may make more stringent conditions for sale o hearing aids.' Thus, those state rules requiring an examination by a audiologist in addition to one by a physician were left intact.

"On May 28, 1977, however, during the comment period for th proposed rules, Congress passed the Medical Device Amendments o 1976. . . . The amendments mandate pre-emption of state and loc requirements with respect to medical devices (including hearing aid that are 'different from, or in addition to' any requirements e tablished by the FDA. . . . The amendments do allow the FDA, b regulation issued after notice and an opportunity for an oral hearin to exempt a state or local medical device requirement from pr emption under such conditions as the FDA may prescribe if the r quirement is (1) more stringent than the federal requirements a plicable to the device, or (2) required by compelling local conditio and compliance with it would not cause the device to be in violation o any other federal requirement. . . . On June 4, 1976, the FD published in the *Federal Register* a notice of the new amendments, 4 *Fed. Reg.* 22620 (1976), but it made no mention of either the effect o the amendments on the proposed hearing aid rules or the FDA's i tention to issue any regulations governing exemption.

"The hearing aid rules were promulgated in final form on Februar 15, 1977, to become effective on August 15, 1977. 42 *Fed Reg.* 928 (1977). The requirement of prior examination by a physician wa retained, but, due to the intervening enactment of the Medical Devic Amendments, the allowance for differing state and local regulatio was deleted.

"Plaintiff ASHA filed petitions for stay and for reconsideration o the final rules with the FDA on March 17, 1977, thus exhausting i administrative remedies. The petitions were denied June 14, 1977, an on the same day the FDA issued proposed rules for exemption of stat medical device requirements. . . . Final exemption rules have not y been promulgated.

II.

"Plaintiffs argue that promulgation of the rules was so fraught wit procedural irregularity that the rules must be reproposed and mad subject once again to a comment period. The crux of the argumer centers around passage of the Medical Device Amendments midwa through the comment period for the proposed rules. The amendments' pre-emption of all state regulation of hearing aid devices i said to have so changed the proposed rules that the regulatory schem as adopted was no longer the same as that originally propose Therefore, the argument continues, the FDA violated both the APA 5 U.S.C.§553 (1970), and its own regulations, 21 C.F.R.§10.40(b)(2 (1977), in failing to (1) issue a notice drawing attention to the intervening legislative change, and (2) extend the comment period t provide a full 60 days after the enactment of the amendments for submission of comments.

"Plaintiffs agree that unless the amendments wrought a 'major substantive difference' between the regulation as proposed and as u timately adopted, there was no requirement of notice or of an extension in the comment period. . . . In this case, unlike those cited b plaintiff, the regulatory scheme itself remained intact; at most th amendments altered only the scope of the rules by automatically pre empting, at least temporarily, the laws of certain states that otherwise would have been exempt. It is questionable whether this type of change qualifies as a 'substantive difference.' It is also questionable whether it can be considered to have been 'major.' Under the rules as originally proposed those states with more stringent requirements would have been automatically exempt from the rules. Now those same states are eligible for exemption upon application to and consideration by the FDA. The difference appears to be largely one of temporary delay.

"Even assuming that the change could be considered to have worked a 'major substantive difference,' no procedural violation occurred. Neither the APA nor any authority cited by plaintiff required an agency to publish in the *Federal Register* notice that an act of Congress has been passed or an analysis of its impact on rules under consideration. 'The statute itself is notice to all' of its provisions and impact. . . . Plaintiffs seek to avoid the operation of this maxim by pointing out, first, that subsequent to passage of the amendments the FDA did issue a notice regarding the effect of the amendments on the proposed rules but failed to mention the pre-emptive effect and, second, that the proposed pre-emption provision was merely 'a gratuitous piece of legal advice' that actively misled parties interested in the regulation after the amendments were adopted. FDA's failure to give notice, although unfortunate, does not rise to the level of reversible error. There is no evidence that anyone was misled. All of the comments received by FDA after enactment of the amendments, including the comment submitted by ASHA, concerned the question of pre-emption, and all correctly interpreted the effect of the new statute.

"Nor is there any violation in the FDA's failure to extend the comment period. Twenty-four days remained after the amendments were passed. The APA, 5 U.S.C.§553 (c) (1970), requires only that interested persons be given 'an opportunity' to comment on proposed rules. FDA's own regulations suggest 60 days for comment but require no more than 10. 21 C.F.R.§10.40(b)(2) (1977). The agency had provided 60 days from the time it promulgated the proposed rules. Even without an extension, 24 days remained in the comment period after passage of the amendments. This was sufficient to satisfy both the APA and FDA's own regulations. It is interesting to note that of the 500-odd comments received by the FDA on all aspects of the hearing aid regulations, only five were received in the last 24 days, thus suggesting that the interested public had long since exhausted its comments. Moreover, FDA's regulations provide for extension of the comment period upon application to the FDA Commissioner by any interested person who shows proper cause. . . . Had plaintiffs felt the need for an extension of time subsequent to enactment of the amendments, this procedure was readily available to them.

III.

"Plaintiffs' attack on the hearing aid regulations is not limited to alleged procedural irregularities, but extends to the substance of the rule as well. The substantive question centers around §801.421(a), which requires, unless waived, a medical evaluation by a physician of the individual suffering from a hearing disorder prior to the sale of a hearing aid. Plaintiffs contend that the requirement that the pre-sale evaluation be conducted by a physician rather than by any practitioner licensed to administer hearing aid devices violates an express provision of the Medical Device Amendments and in any event is arbitrary and capricious.

"At the very heart of the substantive dispute is the fact that FDA's requirement of examination by a physician as opposed to an audiologist has threatened an important facet of the audiologist's role in the hearing aid delivery system. For this reason it is helpful, in evaluating the strength of plaintiffs' claim, to understand something of the audiologist's function. A clinical audiologist is a graduate-school-trained 'individual qualified to provide professional assistance concerning communication problems associated with hearing impairment.' 41 *Fed. Reg.* 16757 (1976). Such assistance includes prevention, identification, evaluation and rehabilitation of people with auditory disorders. Approximately 95 percent of all practicing audiologists are members of plaintiff ASHA, which requires that all members who offer clinical services meet certain qualifications a pass certain tests. Twenty-nine states license audiologists, who m work alone, in conjunction with or under the supervision of a doct or in a school or clinic. By and large they do not sell or install hear aids, and in any event are prohibited by their Code of Ethics from tracting a profit from these services. Ordinarily an audiologist w diagnoses an individual's need for a hearing aid will perfo diagnostic tests to determine the nature of the hearing problem a the proper qualities a hearing device should have. The individual free to approach a hearing aid dealer of his choice. The hearing dealer will perform other tests, make an ear mold, and fit the hear aid.

"Section 2 of the amendments . . . provides in relevant part: T Secretary may by regulation require that a device be restricted to sa distribution, or use . . . (A) only upon the written or oral authori tion of a practitioner licensed by law to administer or use such device, or (B) upon such other conditions as the Secretary m prescribe in such regulation, if, because of its potentiality for harm effect or the collateral measures necessary to its use, the Secreta determines that there cannot otherwise be reasonable assurance of safety and effectiveness. Plaintiffs argue that the regulation in qu tion is invalid under subsection (A), which, in plaintiffs' opinion, quires any regulation mandating pre-sale authorization by a licens practitioner to apply equally to all licensed practitioners. In m states audiologists, physicians, and hearing aid dealers are all licens practitioners within the meaning of the statute. Thus, under subs tion (A), it is argued, a rule requiring authorization by a physician invalid because it excludes other licensed practitioners.

"Plaintiffs' argument has several flaws. First, it is incorrect characterize it as one of exclusion: neither audiologists nor dealers a barred from doing anything, nor are they deprived of their status practitioners. Second, at least in the context of hearing aid sal plaintiffs' construction of the term 'practitioner' leaves subsection (devoid of meaning. Hearing aids are always sold by 'licensed pra titioners' who, by the very act of selling have 'authorized' the sa The type of restriction comprehended by plaintiffs' interpretation subsection (A) imposes no restriction at all. Courts are admonish against construing a statute so as to deprive it of effectiveness meaning. . . . To do so the Court must find that subsection (A) pe mits the FDA to distinguish among different types of practitione and thus to authorize the type of regulation at issue.

"This result accords with plain sense. The purpose of the amen ments was to empower the Secretary or his designate to root out t abuses extant under state regulation of medical devices. . . . T regulation at issue is so obviously directed toward that goal that t Court would have to ignore the most fundamental tenets of statuto interpretation to void it. . . . Plaintiffs' narrow argument does n commend such a course.

"Plaintiffs argue next that even if the regulation does not viola section 2 of the amendments, it is nonetheless arbitrary and capricio and thus voidable under section 10 of the APA, 5 U.S.C.§706(2)((1970). Under the amendments the regulation is valid only if 'the cannot otherwise be reasonable assurance of [the] safety and effe tiveness' of hearing aid devices. Yet if this is so is it not irrational make the examination requirement waivable in a large number cases? And is it not irrational to allow the required examination to performed by any physician, a class that includes podiatrist gynecologists and others with little familiarity with hearing disorder yet at the same time exclude audiologists, whose expertise is in th area?

"These are thoughtful questions. The record shows, however, th they were carefully considered by the FDA prior to enactment. Th regulation is accompanied by detailed and conscientious findings fact that justify the rule adopted. The seeming contradictions are a tually the result of compromises between the competing demand economy and safety. After extended and careful study, the FD found a medical evaluation to be essential for proper diagnosis an treatment. It also found that audiologists were unable to 'differen tiate, diagnose, evaluate and treat the medical cause or causes of hearing impairment.' 42 Fed. Reg. 9288 (1977). Examinations wer authorized by all physicians because of the scarcity of otologist otolaryngologists and other physicians specializing in hearing disorders. A required audiological examination in addition to that of physician was rejected as too expensive and of dubious incrementa benefit. The waiver provision was included to accommodate certai religious and personal beliefs as well as those with the most limite access to physicians. Those eligible to waive the examination may d so only upon signing a form strongly advising against waiver. Th court is far from convinced of the wisdom of the compromise adopted, but is mindful of the limited scope of its review and the deferenc due to the 'informed experience and judgment of the agency to whom Congress delegated appropriate authority.' . . . Because th regulatory choice made in this case cannot be termed unconsidered, i is upheld.

"Finding plaintiffs' arguments inadequate as a matter of law t void the hearing aid regulations, the court hereby denies plaintiffs motion for summary judgment and grants summary judgment t defendants."

ASHA appealed the grant of summary judgment to the government. However, pursuant to stipulation of the parties, the appeal wa dismissed. (Misc. No. 444; N.J. No. 50)

Hearing aid devices, professional and patient labeling and conditions for sale and FDA regulations, at Lauderhill, S. Dist. Fla.

Charged 8-1-77 by Morris Levin, an individual in the hearing ai business, against FDA Commissioner Donald Kennedy, in a complaint for injunction: that U.S. residents could purchase, without physician's written permit, cigarettes, alcholic products and sportin equipment for golf, tennis and bowling, although thousands died annually from problems incurred in the use of such products; that FD regulations on Hearing Aid Devices [which required a physician' written medical evaluation, unless waived] were discriminator towards the plaintiff and others like him in the same business an were in violation of the equal rights granted in the 14th amendment t the Constitution; and that an injunction should be issued to preven enforcement of the regulation.

The government moved to dismiss on the grounds of failure to stat a claim upon which relief could be granted. The court agreed with th government and dismissed the plaintiff's complaint, saying:

"This cause is before the court on the motion of defendant Dr Donald Kennedy to dismiss plaintiff's complaint for failure to state claim upon which relief may be granted. Plaintiff Morris Levi alleges in his complaint that he is being denied equal protection of th law in violation of the 14th Amendment in that defendant as Commissioner of the Food and Drug Administration has issued regulations concerning the hearing aid industry of which plaintiff is a member, 21 C.F.R.§§801.420 and 801.421, but has not issued such regulations in regard to other more dangerous industries. With all du regard to plaintiff's *pro se* status, *Haines* v. *Keiner*, 404 U.S. 51 (1972); *Guerrera* v. *Hauck*, 502 F.2d 970 (5th Cir. 1974), the cour agrees with defendant's assessment of plaintiff's complaint and sha dismiss it.

"Plaintiff does not contend that the FDA lacks authority to issu regulations concerning hearing aids and indeed there can be littl question that the FDA does have explicit statutory authority to do so 21 U.S.C. 371(a), 360j(e), 360(i), 352(f), 352(a), 321(n). There is als little question but that the authorizing statutes have a legitimat governmental purpose, the protection of the public health. *Unite States* v. *An Article of Drug . . . Bacto-Unidisk*, 394 U.S. 784 (1969)

"Plaintiff, of course, is incorrect to invoke the 14th Amendment a the basis of his claim because that amendment is applicable only t state action, *United States* v. *Price*, 383 U.S. 787 (1966) and not t action by the federal government. *Taylor* v. *United States*, 320 F.2 843 (9th Cir. 1963). It is true, however, that the due process clause c the 5th amendment has been held to incorporate the conception c equal protection contained in the 14th Amendment. *Bolling* *Sharpe*, 347 U.S. 497 (1954) and the mode of analysis employed b the Supreme Court in analyzing 14th Amendment and 5th Amendment equal protection cases is precisely the same. *Weinberger* *Wiesenfeld*, 420 U.S. 636 (1975). The court, therefore, shall procee on the assumption that plaintiff intended to invoke the 5th Amendment.

"In the area of social and economic legislation the courts have always used the traditional 'rational basis' standard in determining whether legislation or administrative regulation pursuant thereto was permissible under the concept of equal protection. *Dandridge* v. *Williams*, 397 U.S. 471 (1970). This standard simply stated holds that if a given classification of a statute or regulation is rationally related to a legitimate governmental purpose that classification is permissible. *City of New Orleans* v. *Duke*, *427 U.S.* 297, 96 S.Ct. 2513 (1976). Under this standard legislative classifications are effectively entitled to a presumption of reasonableness and constitutionality and discriminatory classifications will be sustained if any state of the facts can reasonably be said to justify the classification. *Allied Stores of Ohio, Inc.* v. *Bowers*, 358 U.S. 522 (1950).

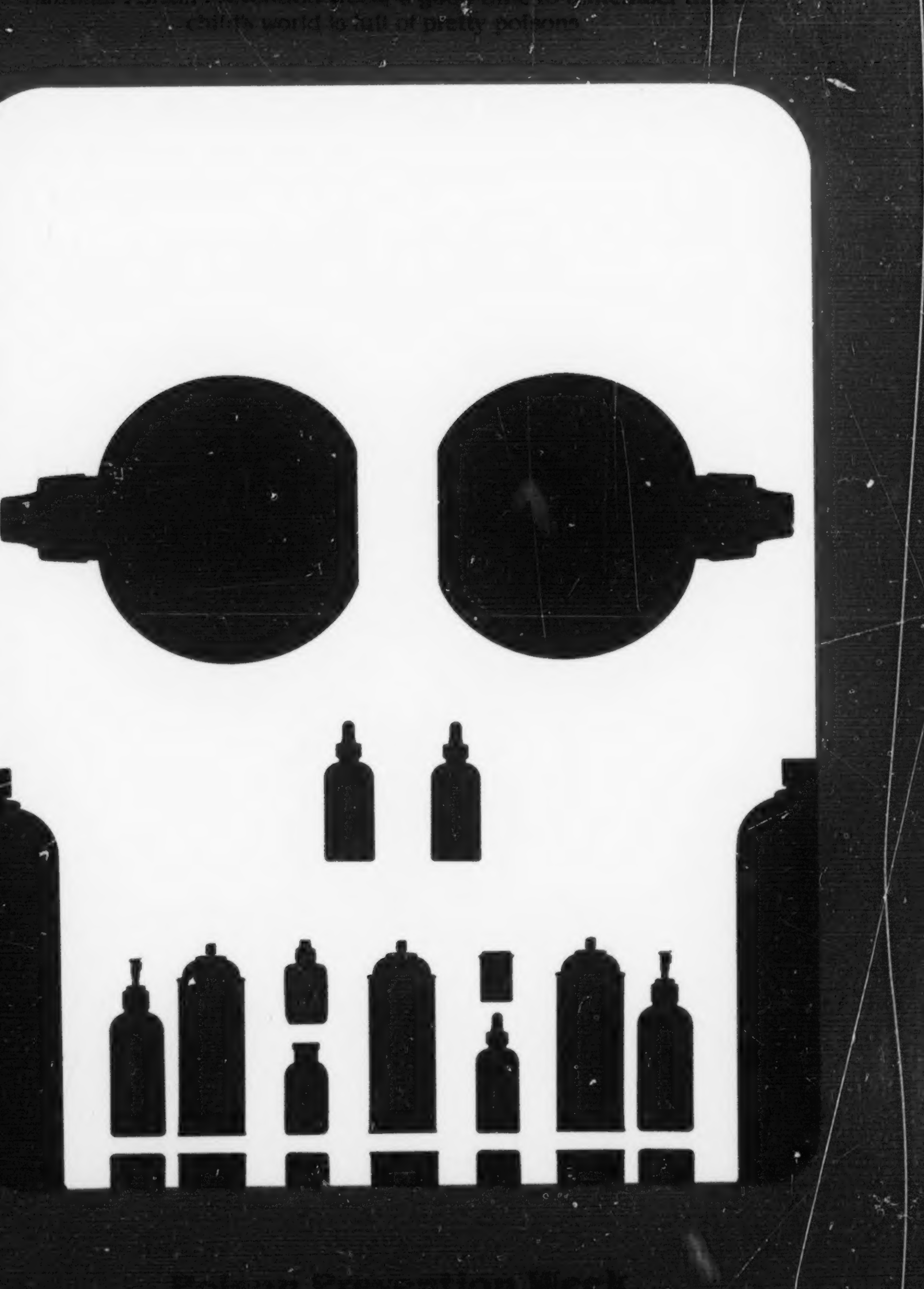
"The regulation of hearing aids seems an almost paradigmatic example of social and economic legislation and the court shall apply the rational basis standard. Giving plaintiff the benefit of the doubt the classification involved in the instant regulation is the classification between individuals in the hearing aid industry who are regulated by the FDA and those individuals in other industries who might be so regulated but are not so regulated. Such classification under the traditional standard is not irrational so long as the regulation involved aims at the achievement of a permissible governmental purpose because the legislature or, as here, the agency might reasonably believe that a solution to the public health problems of the hearing aid industry is possible now whereas the problems of other industries require more time or money to solve. It might reasonably believe that an attempt to solve all problems would result in the solution of none and the defeat of the government's purpose in the regulation of any industry. It is firmly established that reform may proceed step-by-step. *Williamson* v. *Lee Optical of Oklahoma*, 348 U.S. 483 (1955). Accordingly, as the court has already found as a matter of fact that a legitimate governmental purpose is involved in the instant case, the court finds that the classification in the instant case is rationally related to a legitimate governmental purpose and that the defendant has not violated plaintiff's right to equal protection. Accordingly, it is ordered and adjudged that defendant's motion to dismiss is granted and that plaintiff's complaint is dismissed." (Misc. No. 448; N.J. No. 51)

Notices of Judgment are given pursuant to section 705 of the Federal Food, Drug, and Cosmetic Act. Notices of Judgment report cases involving seizure proceedings, criminal proceedings, and injunction proceedings. Seizure proceedings are civil actions taken against *goods* alleged to be in violation, and criminal and injunction proceedings are against *firms* or *individuals* charged to be responsible for violations. The cases generally involve foods, drugs, devices, or cosmetics which were alleged to be adulterated or misbranded or otherwise violative of the law when introduced into and while in interstate commerce, or while held for sale after shipment in interstate commerce.

Notices of Judgment are prepared by Food and Drug Division, Office of the General Counsel, HHS.

Published by direction of the Secretary of Health and Human Services.

Arthur Hull Hayes Jr., M.D., *Commissioner of Food and Drugs*
Washington, D.C., March 1, 1982


Child's world is full of pretty poisons

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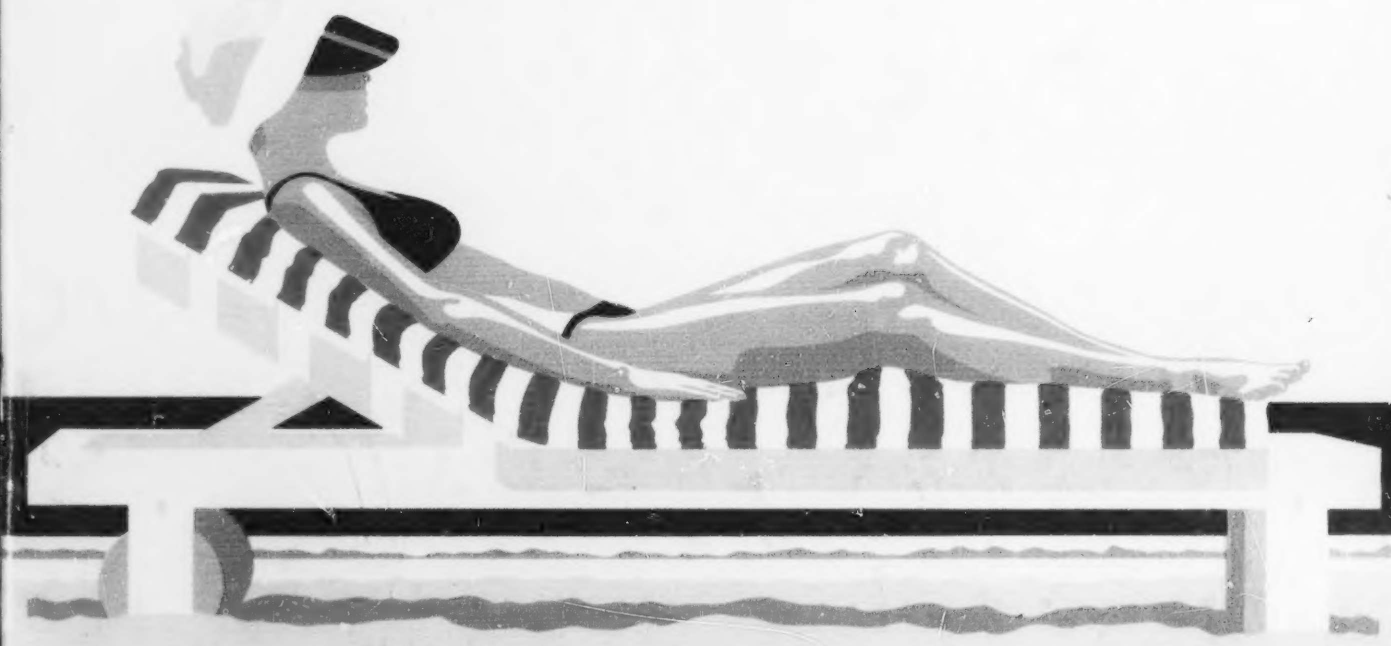

Tan Now, Pay Later?

HE 20.4010:

FDA
CONSUMER

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The Body Doesn't Always Take Kindly to Breast Implants 4
More than 90,000 breast implants are performed annually with silicone. Sometimes this strictly cosmetic surgery can lead to problems.

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A sun tan is considered a healthy look, but the facts are that the sun plays havoc with the skin and can even cause cancer.

Does Your Medicine Chest Need First Aid? 12
For too long has the medicine chest been taken for granted. Often it is located in the wrong place and stocked with the wrong materials.

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These squishy, translucent pillows are actually silicone implants of the type used in thousands of breast enhancement operations each year. Silicone envelopes filled with silicone gel are in the foreground. Empty envelopes that will be filled with saline, using the needle and catheter shown in the center, appear in the background. For more on silicone implants and the body's reactions to them, see The Body Doesn't Always Take Kindly to Breast Implants *beginning on page 4.*

Richard S. Schweiker
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Commissioner of Food and Drugs

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Section 705 [375] of the Food, Drug, and Cosmetic Act:
(a) The Secretary shall cause to be published from time to time reports summarizing all judgments, decrees, and court orders which have been rendered under this Act, including the nature of charge and the disposition thereof.
(b) The Secretary may also cause to be disseminated information regarding food, drugs, devices, or cosmetics in situations involving, in the opinion of the Secretary, imminent danger to health, or gross deception of the consumer. Nothing in this section shall be construed to prohibit the Secretary from collecting, reporting, and illustrating the results of the investigations of the Department.

Cover Design: Zeb Rogerson

Updates

Feingold Diet Limited

The so-called Feingold diet, widely used to treat hyperactive children, should not be universally applied at this time, a panel of experts recently concluded. While recognizing that an initial trial or continuation of the diet may be warranted in patients who seem to benefit, the group said dietary treatment should not be started until after a thorough and appropriate evaluation of the child and his family and full consideration of all therapeutic options.

The 13-member panel, representing a wide range of medical specialties including biomedical research, pediatrics, immunology, clinical pharmacy and the behavioral sciences participated in a National Institutes of Health Consensus Development Conference in early January. The conference focused on the following: a definition of hyperactivity, what constitutes a "defined diet," any evidence that the diet works, a possible explanation of how it works, when the diet should be used, and finally, directions for research.

Hyperactivity is not a single disease nor is there a single cause, the panel noted in the draft of its conclusions. According to the American Psychiatric Association, the essential features are "signs of developmentally inappropriate inattention, impulsivity and hyperactivity." Other diagnostic conditions include onset by the age of 7, duration of no less than six months and a proven absence of mental illness or mental retardation.

The diet introduced by Dr. Ben Feingold in 1973 eliminates two groups of food: those with high levels of naturally occurring salicylates (almonds, cucumbers, tomatoes, berries, apples, oranges) and those containing artificial colors and flavors. Other defined diets are modifications of the Feingold diet.

Dramatic improvements have been observed in many hyperactive children on these diets, the panel said, but such improvements were not established in the controlled trials presented to them. Since there was insufficient evidence to identify the small group of children who do respond to the diet, the panel said it cannot answer unequivocally the question of when the diet should be used.

The group called for more epidemiological research including the development of standardized diagnostic criteria, studies of the causes and risk factors for hyperactivity and research on its natural history. Investigation of family dynamics also is essential, the group said.

The Consensus Development Conference on Defined Diets and Childhood Hyperactivity, part of a program started at NIH in 1977, was co-sponsored by the National Institute of Allergy and Infectious Diseases and the National Institute of Child Health and Human Development.

A fuller explanation of the Feingold diet and how it is perceived to work was the subject of "Food Additives and Hyperactive Children" in the March 1977 *FDA Consumer*. A brief summary of a study done for FDA's Interagency Collaborative Group on Hyperkinesis which tended to refute the Feingold theory appeared in the Update section of the May 1979 issue.

Laetrile: Ineffective, Toxic

The latest word on Laetrile, the controversial drug made from apricot pits, is that it is not effective as a cancer treatment but is toxic and poses a danger to patients. These were the conclusions from a National Cancer Institute study announced last April and reported in January

In the study, 178 patients with cancer but in good general condition received Laetrile and the diet usually prescribed with it. "No substantive benefit was observed," the scientists, headed by Charles G. Moertel of the Mayo Clinic, say. They add that although Laetrile has been advertised to the public, state legislatures and courts as non-toxic, "our results demonstrate that oral Laetrile is a toxic drug. Several patients had symptomatic toxicity or high levels of blood cyanide or both; the cyanide levels approached levels known to kill animals and reached levels that have been reported in fatal cases of poisoning in human beings."

Precautions against fatal poisoning were built into the institute study, the scientists say, but have not been incorporated into the practices of Laetrile therapists who, indeed, sometimes encourage double dosing or other practices that could increase the risk of poisonings. "Physicians using such products must accept the associated liabilities," the scientists warn.

"Certainly, the now established toxicity of Laetrile must be considered by persons in state legislatures and the federal courts who are charged with protecting the public safety."

About half of the states have laws making Laetrile legal within their borders, and Laetrile has been available nationally under an affidavit system established by the District Court for the Western District of Oklahoma to patients who are certified by their physicians to be terminally ill. FDA has been seeking review (and elimination) of the affidavit system.

Laetrile has been the subject of a number of articles, Updates and news items. The most recent article was "The Courts, Terminal Patients and Unapproved Drugs" in the November 1979 issue of *FDA Consumer*.

New Drugs Listed

FDA approved 27 "totally new" drugs last year—the most new chemicals approved for use as drugs since enactment of the 1962 legislation governing drug approval.

The category of new drug chemicals represents one of the most innovative of the six types of new drug approvals. The other types: new salts of previously approved drugs, new dosage forms, combinations, drugs being marketed by a new firm and drugs being marketed for new purposes. How new chemical entities get on the fast track for FDA approval was discussed in "Providing a Breakthrough for Drugs With Promise" in the July-August 1979 issue of *FDA Consumer*.

The 27 new drugs approved in 1981:

Generic Name	**Trade Name**	**Indication**
Albuterol	Schering's Proventil	Bronchodilator
Alprazolam	Upjohn's Xanax	Anti-anxiety
Alprostadil	Upjohn's Prostin VR	Palliative therapy to maintain ductus arteriosus in newborns
Amiloride hydrochloride	Merck's Midamor	Anti-hypertensive
Atenolol	ICI Americas' Tenormin	Anti-hypertensive
Bethanidine sulfate	A. H. Robins' Tenathan	Anti-hypertensive
Buprenorphine	Eaton's Buprenex	Narcotic analgesic
Captopril	Squibb's Capoten	Anti-hypertensive
Cefotaxime sodium	Hoechst-Roussel's Claforan	Antibiotic
Ceruletide	Adria's Tymtran	Anti-ulcer
Estramustine phosphate sodium	Hoffmann-LaRoche's Emcyt	Anti-neoplastic
Flunisolide	Syntex's Nasalide	Symptoms of seasonal rhinitis
Gemfibrozil	Warner-Lambert's Lopid	Lipid regulating agent
Halazepam	Schering's Paxipam	Anti-anxiety agent
Isosulfan blue	Hirsch Industries' Lymphazurin	Lymphatic contrast agent
Ketoconazole	Janssen's Nizoral	Anti-fungal (internal)
Mezlocillin	Miles' Mezlin	Antibiotic
Moralactam disodium	Lilly's Moxam	Antibiotic
Nifedipine	Pfizer's Procardia	For angina
Piperacillin sodium	Lederle's Pipracil	Anti-bacterial
Saralasin acetate	Norwich-Eaton's Sarenin	Detection of angiotension II-dependent hypertension
Secretin	Kabi Group's Secretin-Kabi	Pancreatic diagnostic
Sucralfate	Marion's Carafate	Anti-ulcer
Sulfadoxine (Pyrimethamine)	Hoffmann-LaRoche's Fansidar	Anti-malarial
Temazepam	Sandoz's Restoril	For insomnia
Trazodone	Mead Johnson's Desyrel	Anti-depressant
Verapamil	Knoll's Isoptin and Searle's Calan	Supraventricular tachyarrhythmias

The Body Doesn't Always Take Kindly To Breast Implants

by Paul Tilton and Louise Fenner

Every year thousands of women undergo cosmetic surgery to enlarge their breasts. The results can range from very rewarding to painfully disappointing. Surgery is the only method promoted for breast enlargement that can produce results—unlike the potions, suction devices and exercise machines advertised in many magazines—but it also carries some risks. Women who are aware of these risks will be better able to decide whether surgery is right for them.

The use of surgical techniques to enlarge the breasts is not a new idea. Many methods have been tried since the early 1900s, but only one has been successful—implanting a silicone envelope containing saline or silicone gel under the breast tissue or muscle. Since silicone implants arrived on the medical scene 20 years ago, they have become so widely accepted that an estimated 72,000 surgical breast augmentations take place in the United States every year. The American Society of Plastic and Reconstructive Surgeons based this estimate on a 1980-81 membership survey. Breast reconstructions following mastectomies (breast removals) account for another 20,000 implant procedures annually.

Other than breast reconstruction patients, women who receive silicone implants have healthy breasts that they believe are too small or otherwise undesirably shaped. Some may have breasts that shrank following weight loss or pregnancy or that do not match in size. Others may desire larger breasts for personal or professional reasons—showgirls, for instance. Many of these women undergo the operation with no complications and are happy with the results. However, problems arising from the body's reaction to the breast implant still cause concern for a significant number of patients—problems that remain unsolved.

In the early years, surgical breast enhancement was fraught with complications. Liquid paraffin, used early in the century, sometimes migrated from breast tissue into arteries and caused obstructions that resulted in blindness and pulmonary embolisms (blood clots in the lungs). There were also reports of inflammatory reactions, necrosis (dead breast tissue) and formation of soft-tissue tumors called granulomas.

In the 1950s and 1960s, some physicians turned to injectable liquid silicone. This material has never been approved by the Food and Drug Administration for use in breast enlargement, not even for experimental purposes. Serious injury and several deaths have been attributed to silicone injections. Reported reactions include severe pain, swelling, lumpiness (formation of nodules in the breasts), discoloration and infection. Surgical removal of the breasts has been necessary in some cases to prevent gangrene or potentially fatal migration of silicone particles from the breasts to the brain, heart or lungs.

Overwhelming evidence of these dangers finally put a stop to the widespread use of liquid silicone for breast enlargement, although cases are occasionally still reported along with the resulting side effects. Manufacturers are prohibited by FDA from selling or promoting liquid silicone for use in the breast. If promoted or sold for this unapproved medical purpose, liquid silicone may be seized and legal action taken against the supplier.

The use of implants to augment breast size began in the 1950s, but the failure rate was high until 1963 when two physicians reported successful results with silicone. Three basic types of silicone breast implants are now in use: the silicone gel-filled, the inflatable envelope and the double lumen. On the market the longest, the gel type implant consists of a seamless silicone envelope filled with silicone gel. It is pliable and provides a natural appearance and feel to the breast when in place.

The inflatable implant consists of a silicone envelope that is inflated with sterile saline (salt water) after insertion behind the breast or muscle tissue. It allows the surgeon to adjust the size of the implant by the amount of saline used. Although the inflatable implant was designed to provide a more "natural" postoperative appearance and feel, it has lost popularity since its introduction in the mid-1960s because of numerous reports of delayed spontaneous leakage.

The third type of implant, the double lumen, is a combination of the other two. It consists of two silicone envelopes, most commonly an inner envelope containing silicone gel, surrounded by a second envelope that is filled with saline at the time of surgery. Variations of this silicone/saline combination are also being tried. This type of implant has been in use five or six years.

Breast implants come in a variety of sizes, but the choice is limited by the degree of stretch that the breast can take. When small breasts have pre-

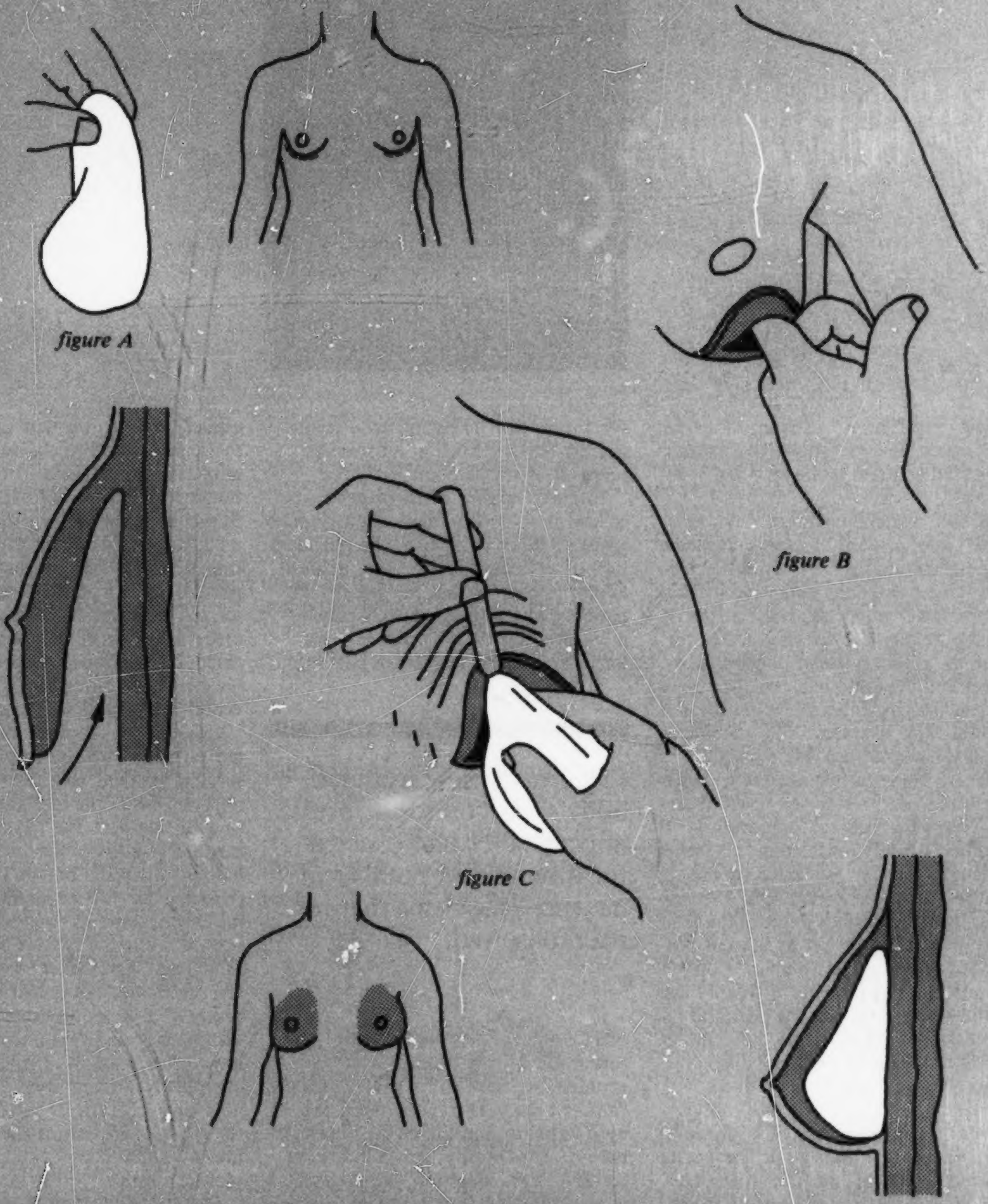


figure A

figure B

figure C

A typical breast implant operation starts with a silicone bag containing silicone gel (figure A), which will be inserted through incisions made in the crease at the bottom of the breast. Once the incision is made, the physician uses a finger to form a pocket between the breast tissue and the pectoral muscle (figure B). With the aid of a retractor (figure C), the implant is inserted into the pocket and positioned carefully. The incision is then closed with stitches.

viously been larger, as from an earlier pregnancy, their elasticity will permit easier adjustment to larger-sized implants.

Breast implant operations can be done under general or local anesthesia. The site chosen for the incision can also vary. Most surgeons make the incision on the lower outer quadrant of the breast, as this affords easy access for forming a pocket between the breast tissue and the underlying pectoral muscle (the breast tissue itself is not cut into or otherwise invaded). The implant is usually inserted into this pocket, although some surgeons place it underneath the pectoral muscle itself. Scarring from the surgical procedure is minimal—rarely longer than 1½ inches in length—and is concealed by the natural fall of the breast. Other techniques include incisions made in the front portion of the arm pit or around the border of the areola (nipple). Complaints by some patients of sensory loss in the nipple area, plus the possibility of invading the breast tissue, have made the areolar method less popular.

As with all surgery procedures, hemorrhage or infection may occur. Hemorrhage may arise from an unnoticed bleeding point or diffuse oozing of blood from the surface of the pectoral muscle. It usually results in the formation of a hematoma, or blood-filled cavity, which appears as swelling and discoloration of the skin. Hemorrhage is rare, but if it occurs the incision is reopened, the implant removed, and the bleeding brought under control.

Infection is another rare but potentially serious complication. It is manifested by pain, fever and redness of the suture line. Infection requires antibiotic therapy and, in most cases, removal of the implant.

Implant surgery often presents special problems because of the human system's defenses against the introduction of a foreign body. Most medical authorities agree that in virtually all patients who undergo breast enlargement procedures, a fibrous capsule forms around the implant as part of the body's natural defense response. The formation of this capsule is not a problem by itself, but in some cases the fibrous tissue contracts around one or both implants and causes the breasts to become unnaturally firm and uncomfortable. This condition, called capsular contracture, has been reported to occur from a few weeks to several years after the surgery.

Problems arising from the body's reaction to the breast implant still cause concern for a significant number of patients—problems that remain unsolved.

Opinions vary widely regarding the incidence of capsular contracture, in part because various physicians may interpret the same symptoms differently. Medical journals have carried articles by doctors who reported contracture rates as low as zero and as high as 74 percent of their patients, although most reports claim rates that fall between these extremes. According to Dr. Norman Hugo, chairman of the American Society of Plastic and Reconstructive Surgeons' public education committee, a capsular contraction rate of 25 percent to 33 percent can normally be expected. Some contractures are characterized by minimal symptoms that include a feeling of tightness and minor discomfort, while in others, the capsule hardens and causes breast distortion (a round "baseball" shape) and pain.

Capsular contracture can be corrected surgically or non-surgically. The surgical method involves removal and replacement of the implant. In the non-surgical method, the physician manually squeezes the breast until the hardened capsule breaks open, thus releasing the silicone implant and allowing it to resume its original shape. This is done while the patient is under sedation. This "nutcracker" technique is often successful, but it can occasionally result in other complications such as hematomas and rupture or displacement of the implant. If the capsule isn't completely broken open, the implant may partially squeeze through cracks in the capsule and distort the shape of the breast. These complications may then require surgical correction.

Once capsular contracture develops, even when later corrected, the rate of recurrence is very high. Medical authorities are uncertain as to why contracture occurs. Theories and techniques are continually being tested, but no methods have been devised to eliminate this problem.

Silicone gel and inflatable implants are known to have some special quirks. Silicone gel-filled implants "bleed"

minute amounts of gel through the surface of the silicone envelope. (This is not to be confused with leakage or rupture.) Small amounts of this silicone bleeding do not appear to be harmful to body tissues, according to studies so far; however, some medical authorities believe additional studies of the chronic long-term toxicity of silicone are needed. One claimed advantage of the double lumen implant is that the outer saline-filled envelope may act as a barrier to gel "bleed" from the silicone-filled inner bag.

On rare occasions silicone-filled implants have ruptured and leaked, and the gel has migrated into adjacent and even distant soft tissue spaces. A hard blow to the breast or erosion of a fold in the silicone envelope are two possible causes of rupture. Cases have been reported when gel leakage into the tissue necessitated removal of part of the patient's breast. Fortunately, such ruptures are unusual, because implants are designed to withstand pressure. In some versions the use of a thicker, more viscous, silicone gel reduces the chance that the gel will migrate into the tissues if the outer envelope breaks.

As noted in the foregoing, inflatable implants have occasionally been known to leak after being in place for some time. In some cases, this occurred as long as 6½ years after implantation. According to published reports, somewhere between 2 percent and 15 percent of all inflatable implants eventually become deflated from various causes. Because saline is compatible with normal body fluids, the leakage itself is not harmful; but additional surgery is required to replace the defective implants.

Because silicone implants have been in use only about 20 years, many questions are unanswered about the long-term effects of breast implant surgery. Other problems that might arise many years after surgery are simply unknown. One question is whether certain materials implanted in the body can increase the long-term risk of causing cancer. To date, there has not been a demonstrated relationship between the silicone implant and the development of breast cancer in humans. However, more extensive long-term patient follow-up studies may be needed before this can be ruled out.

Because silicone implants have been in use only about 20 years, many questions are unanswered about the long-term effects of breast implant surgery.

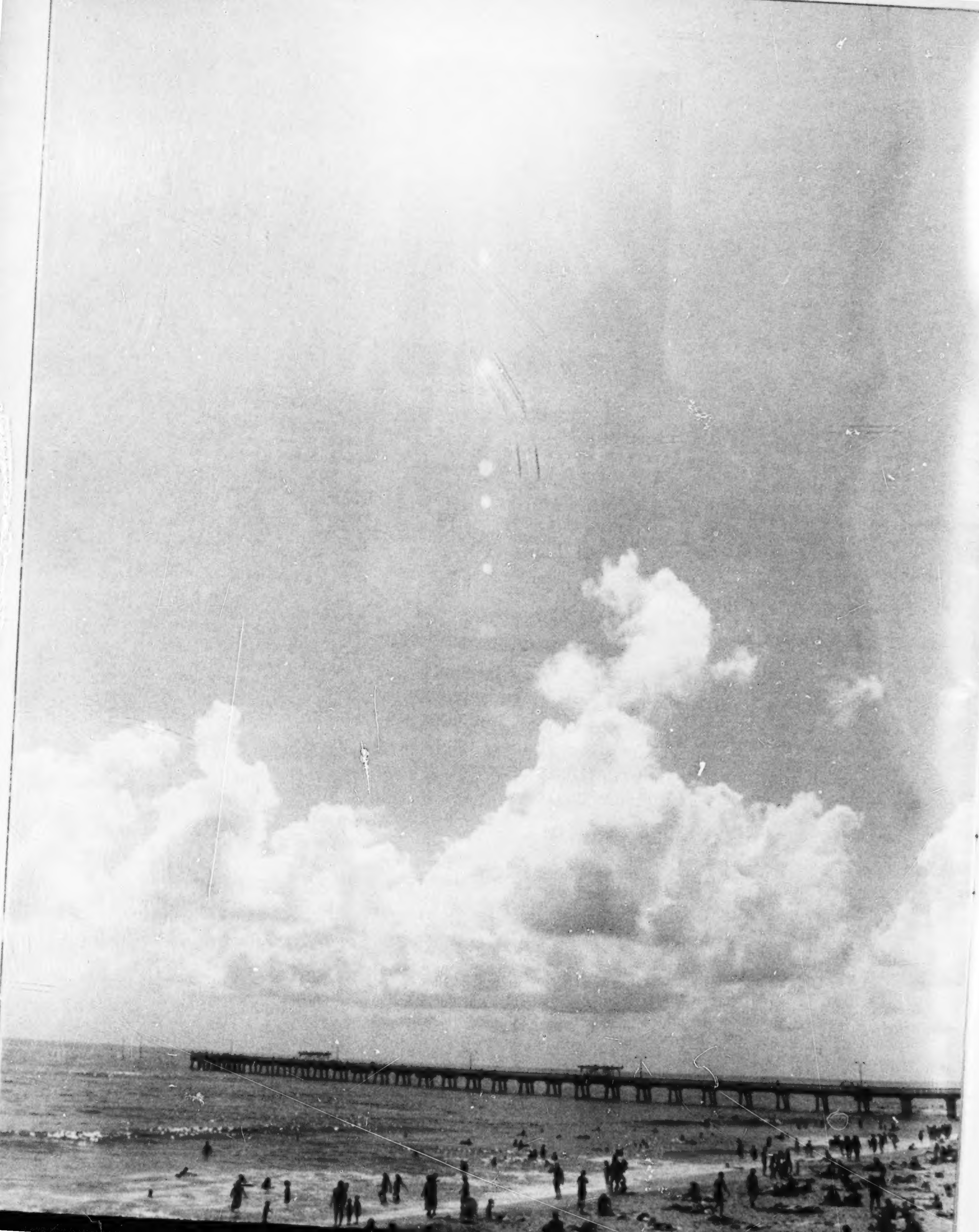
The use of silicone implants for breast reconstruction following cancer surgery has limitations, because a reconstructed breast will not be identical to a normal one. In breast reconstruction, the criterion is generally how a woman looks in a bra or swim suit—not nude—after surgery. Nevertheless, the option is there for the patient. Plastic surgeons are performing successful reconstructions, even in patients who have undergone extensive mastectomies years before.

Silicone implants are regulated by the Food and Drug Administration as medical devices. All silicone implant manufacturers are required to register with FDA and their plants are regularly inspected to determine if they are complying with the Food, Drug, and Cosmetic Act and with FDA's Good Manufacturing Practice regulations. Seven silicone implant manufacturing firms are now registered with FDA.

In January 1982, FDA proposed to classify silicone implants as class III medical devices, a regulatory category requiring premarket approval. (The FD&C Act requires all medical devices to be assigned to one of three categories having varying degrees of regulatory control.) In the classification proposals that appeared in the *Federal Register*, FDA expressed the opinion that not enough information is available about long-term safety and effectiveness of implants to warrant placing them in class II or class I, which have less stringent controls. Final classification decisions will be made after FDA reviews public and industry comments on the proposed classification.

Research continues within the industry, but it is uncertain whether a "perfect" trouble-free implant will be developed because of the basic tolerance problem common to all implants. What's more, each person's reactions to surgery and implantation will be different. Each woman must decide for herself whether it is worth the risk to try to provide what Mother Nature didn't.

Paul Tilton is a biologist in FDA's Bureau of Medical Devices; Louise Fenner is a member of the agency's public affairs staff.



Tan Now, Pay Later?

by Harold Hopkins

In love and romance and other worldly pursuits where personal attractiveness is an asset, one popular method of improving the odds for success is to borrow a bit of coloring from the sun. In other words, get a suntan.

While a suntan—like a kiss—is a temporary thing, some of the undesirable side effects that come with it are longer lasting. The sun damages the skin. Some of the damage may be immediate and obvious: burning and blistering, for example, and various skin rashes or eruptions, as well as eye injury. Other damage may come on the installment plan and may include skin that sags and wrinkles long before it should. Belated damage may also include skin cancer.

Some people are likely to suffer more than others. For many, spending a long time in the sun, when it can be avoided, is rashness beyond reason. Some very fair-skinned people can get severe sunburn from a half hour of exposure in hot summer sun. The elderly, for example, need to take special precautions against overexposure to the sun and high temperatures, as do the obese and people who have diabetes or heart disease. The precaution also extends to people who are taking certain types of drugs, for the sun combined with the drugs can bring on photosensitive or phototoxic effects. A few of the classes of drugs that can create problems when taken along with a heavy dose of sun are certain tranquilizers, anti-emetics (to prevent vomiting), anti-hypertensives, diuretics, tetracycline antibiotics, sulfa drugs, oral diabetic drugs and quinidine. Persons taking any medication, prescribed or over-the-counter, should check with their physicians or pharmacists for possible reactions in strong sunlight.

And when is the sun the strongest? Some lines from a 1932 stage revue tell us the time of day the heat of the sun should be avoided (and also about some kinds of people who fail to heed the advice):

Mad dogs and Englishmen go out in the mid-day sun. . . .
In Rangoon the heat of noon is just what the natives shun. . . .
In Bangkok at twelve
o'clock they foam at the mouth and run. . . .
In Bengal to move at all is seldom if ever done.

There is as much science as whimsy in these lines by Noel Coward for the sun is at its strongest and most harmful during the hours from 10 a.m. to 2 p.m. Anyone wishing to minimize the effects of the sun or to avoid heat stroke would do well to confine his or her sunning to other than mid-day hours.

Ultraviolet radiation is worse at these hours, and it's that type of radiation from the sun that causes sunburns, tans the skin and leaves permanent damage. Excessive ultraviolet radiation will cause hardening and thickening of the epidermis (outer skin) of those who tan readily, and blotching or freckling of the skin of those who don't.

Over the long run, the sun's rays will leave the skin tough, leathery, pebbly and dry. Crow's-feet around the eyes may provide a memento of long hours spent squinting under bright sunlight. Other areas of the body exposed for long periods to the sun's radiation may have surface wrinkles much like those in old shoes. Deep creases around the neck are still another legacy of the sun's ravages.

Skins of individuals are affected differently by the sun. It depends on the amount of the naturally occurring skin pigment, melanin, that an individual's system produces. Persons with darker skins produce larger amounts of melanin. They also tan quicker and with less trouble than those with fair skin. Tanning is especially difficult for those Celtic and other blue-eyed and green-eyed peoples of northern European origins.

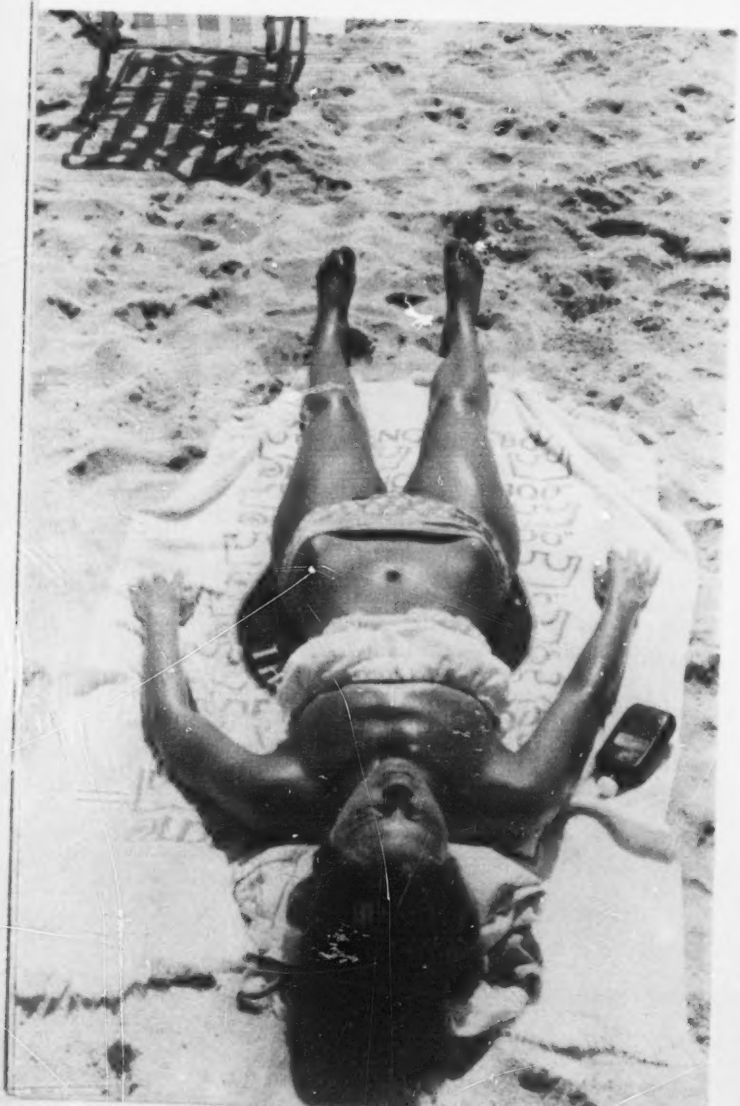
But even those who do tan readily and flaunt their ability to do so may pay dearly for it in the future. Premature aging of the skin is only a part of these deferred payments. The most dreaded long-term effect is the accelerated potential to develop skin cancer.

Ultraviolet radiation from the sun or other sources is the leading cause of skin cancer in people. People who freckle and sunburn easily are especially vulnerable to skin cancer. Most dermatologists consider excessive sunbathing downright foolhardy. They believe the risk of cancer developing from ultraviolet radiation is there, whether one is sunburned or suntanned.

The two most common types of skin cancer—basal cell and squamous cell carcinomas—have been induced in test animals by application of ultraviolet radiation. Each year, according to estimates by the National Cancer Institute, more than 300,000 cases of these two types of skin cancer occur in the United States.

The third type of skin cancer—melanoma—is much more deadly than the others. It has a 40 percent to 50 percent fatality rate, but it is not nearly as common, there being only about 9,000 cases a year. It's not as clear that ultraviolet rays cause melanoma as it is that they cause basal cell and squamous cell cancer, although it's strongly suspected that they do.

Of all types of skin cancer taken together, not more than 2 percent are fatal.



In a 1971-72 study made in several areas of the country by the National Cancer Institute, there were 2.5 times as many cases of non-melanomic cancer in the sunny Dallas-Fort Worth area (latitude 32.8° N) as in the Minneapolis-St. Paul area (latitude 44.9° N), where the sun is less potent. Although skin cancers rarely develop in persons under 20, the incidence increases gradually with advancing age and peaks at about age 75.

The potential for short-term and long-term injury is there whether the ultraviolet radiation comes from the sun or other sources. Sunlamps employing ultraviolet light have long been a favorite for persons seeking a tan in winter or those without access to the sun at other times. More recent has been the popularity, in some parts of the country, of tanning booths or huts, which the customer uses for a fee. All such ultraviolet radiation devices must adhere to FDA design and performance standards, which include requirements for timers, goggles and label directions to help prevent short-term injury.

A panel of scientific experts was engaged by FDA to study a category of over-the-counter drugs that includes sun protectant (screening) products. The panel's report said that liberal, regular use of sunscreen products may help reduce the high incidence of skin cancer and help protect susceptible persons from sunburn. The experts recommended that the labels of such products warn that overexposure to the sun may cause premature aging of the skin and skin cancer and state that sunscreens may provide possible protection against these harmful effects. A minority held that the evidence for sunscreens providing any protection against skin cancer was insufficient and recommended more cautious labeling.

The panel agreed that 21 chemical ingredients marketed in over-the-counter sunscreen products are safe and effective in the prevention of sunburn when properly used. The experts made it clear that they know of no such thing as a perfect prevention for sunburn and said sunscreen products merely extend the time it takes for the sun to cause a burn.

They suggested that sunbathers expose themselves to the sun's rays gradually, while using a suitable sunscreen product.

They recommended that American manufacturers of sunscreen products adopt a numerical system already in use in Europe, called "sun protection factor" (SPF), to designate the relative effectiveness of and the limitations of sunscreens. This numerical rating system in fact is already in wide use among manufacturers in this country and consumers are becoming familiar with and using the system to select sunscreen products to fit their needs.

The rating values are as follows:

- SPF 2 to 4: minimal protection from sunburning; permits suntanning; recommended for people who rarely burn and tan easily and deeply.
- SPF 4 to 6: moderate protection from sunburning; permits some suntanning; recommended for people who tan well with minimal burn.
- SPF 6 to 8: extra protection from sunburning; permits limited suntanning; recommended for people who burn moderately and tan gradually.
- SPF 8 to under 15: maximal protection from sunburning; permits little or no suntanning; recommended for people who always burn easily and tan minimally.
- SPF 15 or greater: ultra protection from sunburn, offers most protection; permits no suntanning; recommended for people who burn easily and never tan.

The range of products marketed under this rating system makes it possible for practically every person to be reasonably well protected from sunburn and to obtain the optimum amount of suntan possible in his or her individual case. Obviously, these screens will not work or will not work as effectively if they are washed off by swimming or diluted by sweating and should be reapplied for safety.

The 21 ingredients the panel found to be safe and effective for use in sunscreen products:

Aminobenzoic acid

Cinoxate

Diethanolamine p-methoxycinnamate

Digalloyl trioleate

Dioxybenzone

Ethyl 4-[bis (hydroxypropyl)] aminobenzoate

2-Ethylhexyl 2-cyano-3, 3-diphenylacrylate

Ethylhexyl-p-methoxycinnamate

2-Ethylhexylsalicylate

Glyceryl aminobenzoate

Homosalate

Lawsone with dihydroxyacetone

Menthyl anthranilate

Oxybenzone

Padimate A

Padimate O

2-Phenylbenzimidazole-5-sulfonic acid

Red petrolatum

Sulisobenzone

Titanium dioxide

Triethanolamine salicylate

Harold Hopkins is editorial director of FDA Consumer *magazine.*

Does Your Medicine Chest Need First Aid?

by Annabel Hecht

A bleary-eyed man rummages through the bathroom cabinet, tossing various bottles and boxes aside until, with a sigh of relief, he finds the remedy for his indisposition.

This scene, enacted frequently in television commercials, may help sell the sponsor's product, but is not one to be recommended for the viewers' home. What's basically wrong with the picture is that the bathroom is not the proper place to store medicines. Bathroom cabinets are usually right over the sink and too accessible to young children. What's more, the warm moist atmosphere of the bathroom can cause some drugs to deteriorate. Not only that, but the clutter Mr. Bleary Eyes found in his cabinet, which obviously made it difficult for him to find what he wanted, suggests that he probably had more drug products there than he really needed.

Of course, it's a good idea to have useful medical supplies on hand for emergencies and to treat minor ills, but the family medicine chest does not have to be a mini drug store. What should be kept in the average household will depend on the makeup of the family. For instance, when there are young children, the medicine chest might include baby aspirin, anti-bacterial topical ointments and medicine to treat symptoms of diarrhea. For that family, syrup of ipecac to induce vomiting and activated charcoal are important for emergency treatment for some accidental poisonings. Persons who are likely to use or administer them, however, should understand the types of poisoning for which they should not be used, as when a caustic agent has been swallowed, for instance.

If there are teenagers, the medicine chest might include acne preparations. An older family member might have a special need for liniment. An adult in reasonably good health may have little use for most over-the-counter medicines.

Generally, medicine chests should include only those health care products likely to be used on a regular basis. A person rarely bothered by constipation, for instance, would have little need for a laxative.

Overstocking drugs in the household should be avoided. Some drug products lose their potency on the shelf in time, especially after they are opened. Other drugs change in consistency. Milk of magnesia, for instance, dries out if it remains on the shelf for a while after opening. Buying the large "family size" of a product not used frequently may seem like a bargain, but it's poor economy if it has to be thrown out before the contents are used up. Ideally, supplies in the medicine chest should be bought to last over a period of no more than six to 12 months.

Obviously, selecting health care items for the family medicine chest is a matter of common sense. Here are some suggested items that will meet the needs of most families:

Non-drug products

Adhesive bandages of assorted sizes

Sterile gauze in pads and a roll

Absorbent cotton

Adhesive tape

Elastic bandage

Small blunt-end scissors

Tweezers

Fever thermometer including rectal type for a young child

Hot water bottle

Heating pad

Eye cup for flushing objects out of the eye

Ice bag

Dosage spoon (common household teaspoons are rarely the correct dosage size)

Vaporizer or humidifier

First aid manual

Drug items

Analgesic—Aspirin and/or acetaminophen. Both reduce fever and relieve pain, but only aspirin can reduce inflammation.

Emetic—syrup of ipecac to induce vomiting and activated charcoal. Read the instructions on how to use these products.

Antacid

Antiseptic solution

Hydrocortisone creams for skin problems

Calamine for poison ivy and other skin irritations

Petroleum jelly as a lubricant

Anti-diarrhetic

Cough syrup—non-suppressant type

Decongestant

Burn ointment

Anti-bacterial topical ointment

The medicine chest might also include anti-nausea medication if any family member is prone to motion sickness, a laxative and some liniment. Seasonal items, such as insect repellents and sunscreens round out the list.

When it comes to storing these health care items the cardinal rule is to keep all medicines out of the reach of children. In addition, be sure all medications have child-resistant caps. Elderly people who have difficulty opening such caps can ask the druggist for regular closure. However, they should be extra careful to see that young visitors can't get to these drugs.

Both prescription and non-prescription drugs should be kept in a cool, dry place away from foods and other household products. Some drugs may need to be kept in the refrigerator. This should be indicated on the label. If in doubt, ask the pharmacist.

Many people keep medicines on a high shelf in a hall or bedroom closet. Some experts suggest using a locking box. A tackle box might do. A word of warning, however: Be sure all responsible adults in the family know where the key is kept.

To avoid confusion keep prescription and non-prescription drugs in separate boxes clearly labeled to distinguish one type of drug from the other. A list of what's in each box, attached to the outside if possible, will make it easier to find specific items, particularly in an emergency.

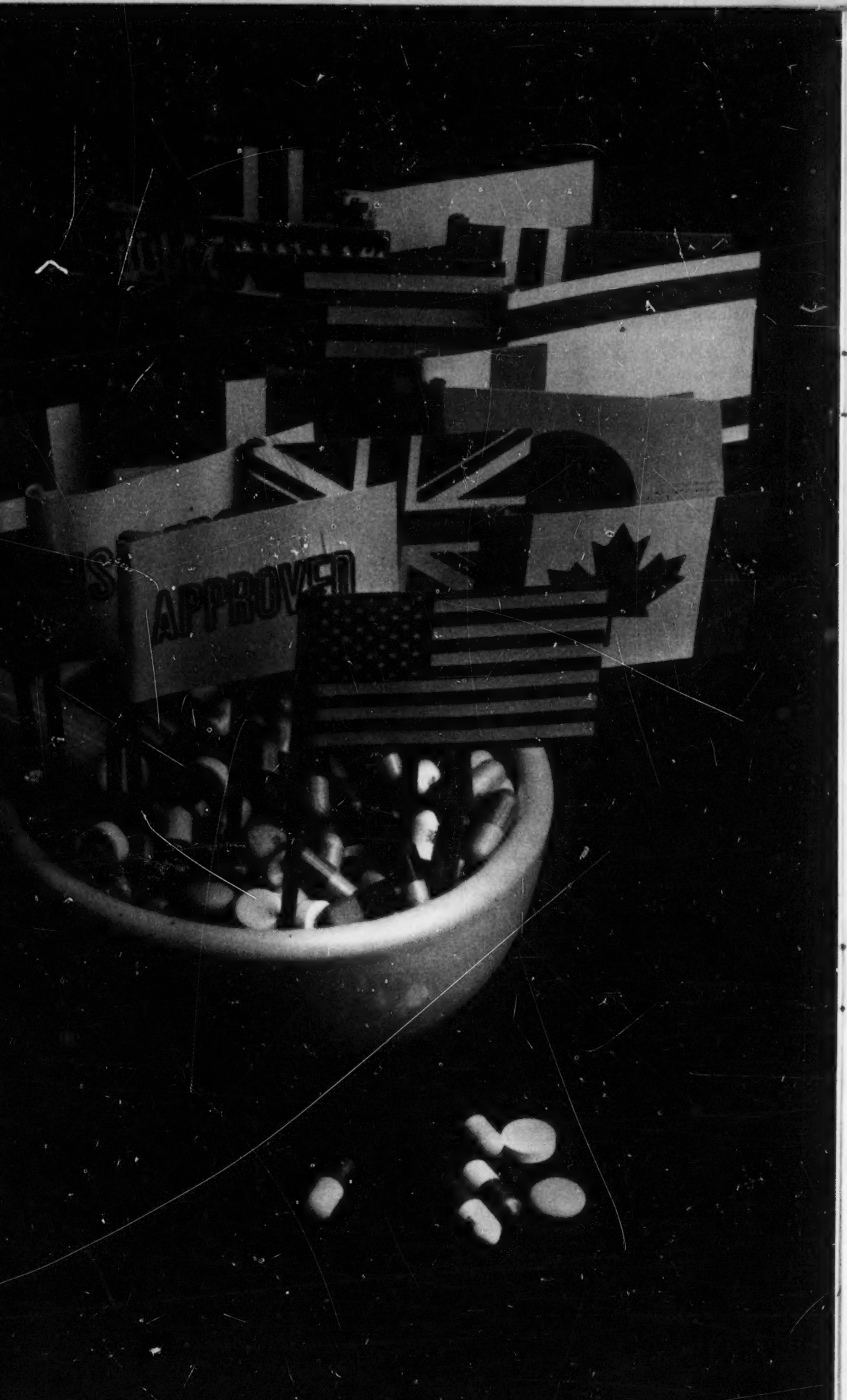
The medicine chest should be checked periodically to be sure supplies haven't run low and to get rid of drugs that may have gone bad or become outdated. Many drug labels have an expiration date beyond which the product should not be used. If there isn't a date, put a label on the container with the date of purchase and the date it was first opened. Then, if there are any questions in the future, a pharmacist can tell whether the product is safe to use.

Tablets that have become crumbly, medicines that have changed color, odor or consistency, or are outdated, should be destroyed. Empty the bottle of medicine into the toilet, flush it down, and rinse out the bottle. Don't put leftover drugs in the trash basket where they can be dug out by inquisitive youngsters. Newly purchased drug products that don't look right should be returned to the pharmacy. Drug products that have lost their labels also should be destroyed.

Keep the telephone numbers of the local poison control center, physician, hospital, rescue squad, fire and police departments near every phone in the house. Tape the emergency phone list inside the bathroom medicine cabinet door and also keep it with the emergency supplies.

Each family's medicine chest is bound to contain some different items. For help in selecting appropriate health care products, check with a physician and a pharmacist.

Annabel Hecht is a member of FDA's public affairs staff.

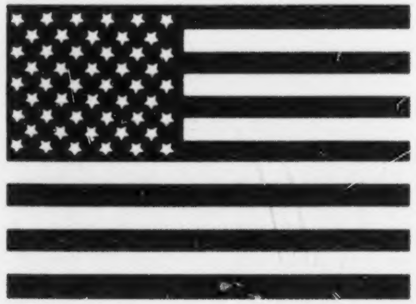


A Global Look At Drug Approvals

by Christopher Smith

Drugs are chemicals or combinations of chemicals that, for the most part, are unusual to the human body. They are allowed to enter into human beings for therapeutic purposes—to cure a disease or minimize its impact, or to restore a lost function. But only some chemicals or chemical combinations should be allowed to enter into the human system. Which should be permitted access and which should be kept out? The answer to that question is deceptively simple: Only those drugs (read: chemicals) that are safe and effective should be given access.

But the average citizen, in the United States or West Germany or South Africa or wherever, cannot make the safety and efficacy decision on a particular chemical. So he must look to the government to do so. Just how the government does that varies by country.



In this country, the drug approval process is divided into two parts: the testing phase and the review phase.

During the testing phase, the Food and Drug Administration requires that animal studies be performed before human testing can begin. If the animal tests indicate that the drug can be used safely in man, and may be therapeutically useful, the drug manufacturer or sponsor submits to FDA a Notice of Claimed Investigational Exemption for a New Drug, called an IND. This filing includes information about the drug's chemical composition, how it is made, and a description of the plan for testing it in humans. Unless FDA raises objections within 30 days, the manufacturer may begin the drug tests.

FDA reviews the IND to make sure that patients will not be subjected to unwarranted risks during the tests and to see that the tests will yield significant results. FDA also monitors these tests and requires that review boards be established in the universities, hospitals and other institutions where the drug research is being done. These institutional review boards, as they are called, are composed of local professional people who are responsible for assuring that patients treated with experimental drugs have given their consent and that the possible benefits are worth the expected risks for the patients who take part in the testing.

In Germany, a law that became effective in 1978 also requires that new drugs be shown to be both safe and effective before approval. There,the Institute für Arzneimittel Bundesgesundheitsamt does the job of approving new drugs. Unlike the U.S. system, no review of the pharmacological and toxicological pre-testing of the chemical is done by the agency before a sponsor is allowed to test the drug in patients. Before beginning, the drug sponsor simply turns over sealed packages to the government describing the results of these tests. The packages are opened only if problems arise at some later time. During this investigational phase, the German institute does not require that institutional review boards be present to help assure the patient's protection.

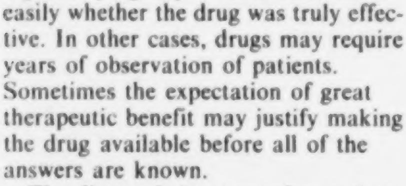
In Canada, the drug approval function is the responsibility of the Health Protection Branch of the National Health and Welfare Department. Just as in the United States, a manufacturer must submit an IND before beginning clinical studies. This IND is reviewed by the authorities for much the same reasons as it is looked at here. A difference exists, however, in the time required for this review. Whereas FDA allows the experiments to begin in 30 days or less, in Canada the drug sponsor usually must wait about 90 days. As with the German system, the Health Protection Branch has no regulatory authority to require review by institutional boards or to require informed consent of the patients in studies of investigational drugs.

Great Britain recently changed its requirements for investigating drugs in humans. A sponsor had been required to apply for a license to study new drugs in patients other than healthy volunteers. The application was complicated and the British regulators took as long as nine months to grant approval for the testing. The drug industry objected to the controls and the Medicines Division of the Department of Health and Social Security responded with a "Clinical Trial Exemption" similar to the IND. Upon filing of the exemption, the

British agency has 35 days to consider the application and advise the company whether it objects to the trials.

Once begun, the time taken to carry out investigational tests on new drugs also varies from country to country. This is not only because of differences in requirements among regulatory agencies, but also because of the nature of the drugs themselves. Very effective drugs that may be beneficial to large populations, such as penicillin for patients with pneumonia, may require testing and careful observation of a limited number of patients before effectiveness can be demonstrated. Drugs of marginal or borderline effectiveness require larger numbers of patients in the clinical studies. In these cases, the larger number of subjects will allow both the drug manufacturer and the regulatory agency to determine more easily whether the drug was truly effective. In other cases, drugs may require years of observation of patients. Sometimes the expectation of great therapeutic benefit may justify making the drug available before all of the answers are known.

The disease being treated can also play a role in the time it takes for the drug's testing. For example, a drug manufacturer obviously must study the effects of a drug for the treatment of a particular tropical disease in countries where that disease is prevalent. Other factors that affect early drug testing are the period the drug will have to be used by the patient; population characteristics such as ethnic background, general health and state of nutrition; and differences in the practice of medicine.

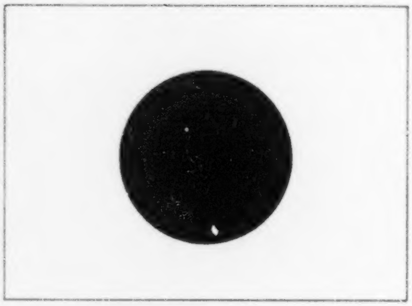


The second major phase of drug development involves the approval of the drug for marketing. In the United States, the application for this approval is called a New Drug Application, or NDA. The NDA contains all the information the sponsor has about the drug and usually runs into thousands of pages. As each application makes its way through the FDA approval process, it is seen by physicians, pharmacologists, chemists and statisticians. In some cases, specialists such as microbiologists may also review the submission. These scientists must ascertain whether the drug is safe and effective, what its labeling should say, and whether the sponsor can manufacture the drug properly. At times, FDA is assisted in this review by 15 advisory committees composed of outside experts in specific drug areas.

In Sweden, this process is carried out by the Department of Drugs. Like the U.S. requirements, Swedish law demands a full report of all studies, including those done outside of Sweden. The data may be summarized by the sponsor and is reviewed by the physicians, pharmacists and chemists of the department in much the same way FDA review teams go over NDAs.

Canada also requires that studies be submitted to document a drug's safety and effectiveness. Many times Canadian authorities review not only summaries of the investigational results but also individual patient records to assure the adequacy of the testing. Like FDA, Canada's Health Protection Branch requires that these studies be well controlled and that they adequately substantiate the claims made for the new drug.

In Japan, new drugs are reviewed in a complicated system of government appointed committees and subcommittees. These outside reviewers comprise 68 committees of senior experts and eminent specialists from universities, hospitals and research centers throughout the country. After the review a recommendation is made to the regulatory agency regarding the drug's approval. No new drug from outside the country can be approved in



Japan unless the drug has been sanctioned for use first in the country of origin. The Ministry of Health and Welfare also requires that certain tests be carried out in Japan before the drug will be considered for approval in that country. The data are then collected and submitted to the committees, usually in a summarized form only. No individual patient records are required.

In some countries, such as Algeria, Bolivia and Uruguay, no guidelines exist to assist the drug sponsor in obtaining licensing approval. Indeed, many countries have no specially designed system to register a drug for the market.

When a manufacturer submits a New Drug Application to FDA, the law allows 180 days for the agency to conduct its review and approve or not approve the drug for marketing. Most NDAs, however, are not approved after this first review cycle because of deficiencies in one or more areas of the application. Eventually about 85 percent of the NDAs are approved, usually after the second or third cycle. The total approval times from initial submission to final approval vary from six months to several years. During 1981 FDA approved 96 New Drug Applications including 27 for chemicals never before used in this country as drugs. FDA's average time for approval of New Drug Applications was shortened from almost three years in 1979 to less than two years in 1981.

In some countries it's fairly easy for sponsors to gain approval for marketing new drugs. This is especially true in many underdeveloped areas of the world such as Latin America and

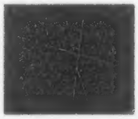
Africa. Approvals generally take longer in countries such as Germany, Sweden, Canada, Great Britain and Japan, which have well-developed regulatory systems. In Sweden, the time period for approval has risen steadily over the last decade and is now 2½ years. The German regulatory agency has four months to decide on approval once the data are submitted. Additional information can be requested of the sponsor and, once that is submitted, the regulations allow three additional months for the review. The average time for approval in Germany is about 10 months. In England, a new drug approval takes about a year. There, the Medicines Division has 120 days in the first cycle but when new information is requested, additional review periods can be allowed.

Canadian law requires that the Health Protection Branch answer a sponsor's request for approval within 120 days. Clearance time for an application after the necessary review and any additional requests by the sponsor is now estimated at about 11 months. Approval in Japan can take from one to three years. Japan has no time limit restrictions.

In most countries approval is accompanied by a licensing arrangement that requires periodic renewal. In Germany and the United Kingdom, registration is granted for five years. The same is true in Czechoslovakia, Israel and Greece. In South Africa, it is one year. In Egypt, licenses are granted for 10 years. Many of the countries also charge fees for relicensing after that period has expired. The United States, Sweden and Canada do not require renewals or charge fees.

Differences also exist among countries in how drugs are monitored once on the market. After a drug is in wide use, the data that show the balance between its benefits and risks may change. Previously undetected adverse effects may be discovered, or particular groups of patients may turn up who are more or less likely to develop adverse reactions. A drug also may be found effective for uses other than those studied before marketing. When new discoveries are made about a drug, its label may need revision. Occasionally, if a very serious reaction to or risk from a drug turns up, removal from the market may be necessary.

Once a drug is approved in the United States, the manufacturer is required to report any newly found adverse reactions. FDA participates in many post-marketing surveillance programs involving drug products, including those operated by the United States Pharmacopeia and the World Health Organization. An FDA system for voluntary reporting by health professionals draws some 12,000 reports of adverse reactions annually. Besides these systems, both domestic and foreign scientific literature are constantly reviewed for reports of adverse reaction incidents.



Germany, Sweden and the United Kingdom also operate post-marketing surveillance systems and have requirements for drug experience reporting by drug manufacturers. Collection of adverse reaction data is easier for British authorities in many ways because that country operates a national health insurance program from which data about drug use are retrieved quite readily.

Many South American countries, as well as Portugal, the Netherlands and Hong Kong, have no legal requirements for reporting adverse reactions by drug firms or for monitoring the use of the products after marketing begins.

In addition to the drug regulatory process, other factors affect the drug approval system: the array of marketed drugs varies, the practices of medicine differ, and the drugs perceived by the industry or by physicians in one country to be worthy of marketing are not the same as those in another. This is why drugs are often introduced in different countries at different times. Just where a drug is introduced may depend on where it was discovered, the research resources available in that country, the disease for which the drug is intended, and the differences in the costs of research in different countries. Also of importance are economic issues such as the value of currency, tax structures and labor costs.

Still other factors that influence drug introduction are differences in the forms of government. In the United States, for example, the government system requires that decision making be for the most part on the record, from congressional hearings to public advisory committee meetings to solicitations for public comment in the *Federal Register*. In addition, the Freedom of Information Act provides access to much of the information on which the drug is evaluated and approved.

Today, the U.S. system for drug evaluation might well be considered at a crossroads. Last September, FDA Commissioner Arthur Hull Hayes Jr. established a task force to conduct a review of the drug approval process. Among the subjects being studied by the group are the amounts of data required by FDA for drug approval, the use of advisory committees, and more use of information from foreign studies. Also being looked at is the handling of so-called breakthrough drugs, those with special promise. In addition, a special committee on the drug approval process has been established by Congress. Consisting of non-government experts, that group will report its findings to the lawmakers.

All of this scrutiny could bode well for the system, as it could result in development of a better way for maintaining the delicate balance between those drugs that are approved too soon and those that arrive too late.

Christopher Smith is a member of FDA's public affairs staff.

How To Ignore Salt And Still Please The Palate

by Roger W. Miller

"People are just overwhelmed with the idea that they have to give up salt. They think they're being penalized. But you just have to withdraw the idea of salt. You have to adjust flavorings—use lemon, garlic and fresh herbs. I've done that with considerable success for years."

That's the advice of James Beard, a food connoisseur who has been writing cookbooks for 40 years and revealing his culinary techniques on television for more than a quarter of a century. It's obvious that a man with these credentials didn't just misplace his salt shaker. No, the reason Beard foregoes salt is that he is a high blood pressure victim who is on a salt (sodium) restricted diet.

Adding spice to Beard's sentiments is Craig Claiborne, food editor of the *New York Times* and author of 14 cookbooks including one that features low-sodium recipes. Claiborne is another hypertension or high blood pressure victim. He had been on drugs to control his pressure, but the drugs didn't work. A low-sodium diet did. Claiborne finds the amount of sodium we add to our food appalling. Today his recipes in the Sunday *New York Times Magazine* invariably include the line:

"Salt, if desired."

Claiborne thinks there are many ways to ignore salt and still "fool the palate," and his thoughts are shared by a number of other authors who have turned out low-salt cookbooks. The authors include other gourmets, doctors, scientists and just plain consumers who found themselves ordered to reduce their salt intake.

Too much sodium (salt is 40 percent sodium) is a problem for the estimated 60 million Americans who have high blood pressure or who are marginal hypertensives. Evidence is mounting that those to whom hypertension is a family affair are more likely to intensify the problem with a high-sodium diet.

Americans consume an estimated 2,000 to 6,000 milligrams (mg) of sodium per day. That's about the same as gulping down one to three teaspoons of salt. Most experts agree that the average adult can get along on 1,000 milligrams or less a day.

Controlling the amount of sodium in the diet is no easy matter. The stuff comes from three sources: some occurs naturally in food and water, some is added in cooking and at the table, and the rest is put into foods during processing for a variety of reasons, mainly for taste and preservation.

The Food and Drug Administration began a major effort in 1981 to enlist the aid of food manufacturers in lowering sodium content and providing better label information of the amounts of sodium in processed foods. In less than a year that effort has paid off with cooperation from such major processors as Del Monte, Quaker Oats, General Foods, Frito-Lay, Beatrice Foods, Campbell Soup, Friday Canning Corp. and Procter & Gamble as well as some supermarket chains such as Stop & Go. Within a year, it is expected that a third of the processed foods regulated by FDA will carry sodium content on their labels. That would be a tripling of such information.

FDA now requires that foods sold as low-sodium items must spell out on the label the number of milligrams of sodium contained in 100 grams of the product, plus the number of milligrams in a serving. To understand this information, the consumer must remember that there are 1,000 milligrams in a gram and 28.4 grams in an ounce.

Waiting in the wings are regulations to define the terms "low sodium," "moderately low sodium" and "reduced sodium" when used on food labels.

Not too much can be done about the sodium Mother Nature adds to her bounty. However, the pots and pans pundits are ready to offer relief from the kitchen use of salt and other high sodium cooking products such as baking soda, monosodium glutamate (MSG) and soy sauce.

For the average consumer, such relief is not spelled e-a-s-y. It's not that the cooking is any more difficult, but low-sodium and sodium-free products continue to be more expensive and harder to find on store shelves. Sometimes it seems that the consumer is being asked to pay for what is left out. In testimony before Congress in April 1981, Claiborne said: "The worst thing about trying to maintain a (low-sodium) diet . . . [is] trying to find foods on the supermarket shelf not containing salt." In reality, the problem is the law of supply and demand. Up to this point there just hasn't been enough demand for those products.

And the book *How To Live 365 Days a Year—The Salt-Free Way* has a chapter titled "High Adventure in the Supermarket: In Search of Low-Sodium Food." That book was written in 1977. One would hope that the situation has improved and will continue to do so. However, the authors advise consumers to ask the store manager for low-sodium and sodium-free products and to voice their displeasure when none is available.

It is unrealistic to expect to find any simple salt substitutes. A number of products labeled "salt substitute" are on the market. They usually contain potassium chloride as a partial or complete replacement for sodium chloride (table salt). Some of the cookbook writers have complained about the substitutes, one saying that they distort the flavors of foods. More important, people with certain medical conditions, such as severe liver or kidney disease, must control the amount of potassium they take in. People with a serious desire or concern about potassium intake for other reasons should consult with their physician before using a salt substitute.

However, as James Beard noted, there are flavorings that can often be substituted for salt, and some of these are natural seasonings for the foods. The American Heart Association's cookbook, *Cooking Without Your Salt Shaker*, offers a simple guide for flavor combinations. That guide is printed in a box adjoining this article. Some of the

How To Ignore Salt

From the American Heart Association's cookbook *Cooking Without Your Salt Shaker*, here's a simple guide for substituting herbs and spices for salt in a variety of foods:

Meat & Fish & Poultry

Beef:	*Bay leaf, dry mustard powder, green pepper, marjoram, fresh mushrooms, nutmeg, onion, pepper, sage , thyme.*
Chicken:	*Green pepper, lemon juice, marjoram, fresh mushrooms, paprika, parsley, poultry seasoning, sage, thyme.*
Fish:	*Bay leaf, curry powder, dry mustard powder, green pepper, lemon juice, marjoram, fresh mushrooms, paprika.*
Lamb:	*Curry powder, garlic, mint, mint jelly, pineapple, rosemary.*
Pork:	*Apple, applesauce, garlic, onion, sage.*
Veal:	*Apricot, bay leaf, curry powder, ginger, marjoram, oregano.*

Vegetables

Asparagus:	*Garlic, lemon juice, onion, vinegar.*
Corn:	*Green pepper, pimiento, fresh tomato.*
Cucumbers:	*Chives, dill, garlic, vinegar.*
Green Beans:	*Dill, lemon juice, marjoram, nutmeg, pimiento.*
Greens:	*Onion, pepper, vinegar.*
Peas:	*Green pepper, mint, fresh mushrooms, onion, parsley.*
Potatoes:	*Green pepper, mace, onion, paprika, parsley.*
Rice:	*Chives, green pepper, onion, pimiento, saffron.*
Squash:	*Brown sugar, cinnamon, ginger, mace, nutmeg, onion.*
Tomatoes:	*Basil, marjoram, onion, oregano.*
Soups:	*A pinch of dry mustard powder in bean soup; allspice, a small amount of vinegar or a dash of sugar in vegetable soup; peppercorns in skim milk chowders; bay leaf and parsley in pea soup.*

Salt-Free Books

Following are some books that people interested in maintaining a sodium-restricted diet may obtain. The list is not meant to be comprehensive in the subject area, nor does the listing constitute an endorsement of the books by FDA or this magazine. They are listed alphabetically by title.

Cooking Without a Grain of Salt, by Elma W. Bragg, Bantam Books, New York, N.Y. Also published in hardback by Doubleday & Co.

Cooking Without Your Salt Shaker, American Heart Association, Dallas, Texas.

Craig Claiborne's Gourmet Diet, Ballantine Books, New York, N.Y. Also published in hardback by Random House.

The Dell Color-Coded Low-Salt-Living Guide, by Janet James and Lois Goulder, Dell Publishing Co., New York, N.Y.

The Dictionary of Sodium, Fats, and Cholesterol, by Barbara Kraus, Grosset & Dunlap, New York, N.Y.

The Dieter's Gourmet Cookbook, by Francine Prince, Cornerstone Library, New York, N.Y.

Dr. Rechtschaffen's Diet for Lifetime Weight Control & Better Health, Random House, New York, N.Y.

Gourmet Cooking Without Salt, by Eleanor P. Brenner, Doubleday & Co., Garden City, N.Y.

How to Live 365 Days a Year the Salt-Free Way, by J. Peter Brunswick, Dorothy Love and Assa Weinberg, M.D., Bantam Books, New York, N.Y.

Living Salt Free & Easy, by Anna Houston Thorburn with Phyllis Turner, New American Library, Inc., New York, N.Y. Also published in hardcover by Douglas-West Publishers, New York, N.Y.

Salt-Free Cooking With Herbs and Spices, by June Roth, Contemporary Books, Chicago, Ill.

Secrets of Salt-Free Cooking, by Jeanne Jones, 101 Productions, San Francisco, Calif.

Sodium Content of Your Food, which is referred to in the article, is available free of charge by sending a postcard to:

FDA Consumer Communications
HFE-88
5600 Fishers Lane
Rockville, Md. 20857

It lists the sodium content of 789 foods and food products as well as a number of popular non-prescription drugs.

The Dieter's Gourmet Cookbook
Francine Prince
The Dell Color-Coded Low-Salt Living Guide
How to Live 365 Days a Year the Salt-Free Way
Gourmet Cooking Without Salt
Salt-Free Cooking with Herbs and Spices
June Roth
The Dictionary of Sodium, Fats, and Cholesterol
by Barbara Kraus
Dr. Rechtschaffen's Diet for Lifetime Weight Control & Better Health
Craig Claiborne says
Living Salt Free & Easy

other cookbooks offer more detailed listings.

Despite Nature's penchant for incorporating sodium in food and water, living on or cooking for a low-sodium diet usually means using fresh vegetables whenever possible. For examples see the U.S. Department of Agriculture's booklet *The Sodium Content of Your Food*. It reveals that a cup of cooked fresh corn contains only one milligram of sodium, while a cup of frozen has seven and a cup of canned 671. The ratios are much the same for most vegetables. Frozen dinners also tend to be high in sodium, according to information supplied by manufacturers to *The Dell Color-Coded Low-Salt-Living Guide*. Most of 14 dinners listed in that book had more than 1,000 mg of sodium, topped by the 1,615 in the fried chicken serving. Most of the sodium is added in the processing.

There are some quirks in the raw-is-good maxim. Celery, for example, runs 25 mg of sodium to a stalk (but less when cooked sans salt because some sodium is lost in the cooking). Likewise, regular milk and fresh meat contain moderately low amounts of sodium. One cup of whole milk has 122 mg, while an ounce of cheddar cheese (to which salt is added in processing) provides 176 mg. Most raw meats are moderately low in sodium, but the sodium counts go up considerably when the meats are corned, smoked, dried, cured or processed in other ways.

Needless to say, fish from salt water runs higher in sodium than fresh water fish. Again, most fish, including frozen forms, are higher when processed. Three ounces of raw shrimp contains about 137 mg. However, when canned it contains 1,955 mg of sodium, according to the USDA publication. And smoked herring runs up to 5,234 mg of sodium for three ounces.

Of course, some other salty items are well known: canned sauerkraut, 1,554 mg per cup; dry roasted, salted peanuts, 986 mg per cup; one dill pickle, 928 mg and a frankfurter, 639 mg.

Not so well known are Manhattan style condensed clam chowder with water, 1,808 mg per cup; catsup, 156 mg for a tablespoon; pancake mix, 2,036 mg in a cup.

The amount of sodium that occurs in a community's drinking water will vary by areas. Usually a call to the local water department will give a quick sodium headcount, a couple of writers noted. *The Dictionary of Sodium, Fats, and Cholesterol* has a state-by-state breakdown of the sodium content of municipal water supplies ranging from Birmingham, Ala. (0.5 mg per cup) to Milwaukee, Wis. (1.0 mg per cup). The highest listing is 46.9 mg/cup for one of the plants serving Long Beach, Calif.

Eating out can present special problems for those who have to restrict their sodium intake. Several of the books offer advice on how to get along on the fewest milligrams while so far from the home range. In *The Secrets of Salt Free Cooking*, the author starts out with this advice about restaurant dining: "The first assumption you must make is that your waiter doesn't know anything about low-sodium diets." From then on, it's a matter of choosing foods wisely, avoiding known salty items such as soups, most sauces and salad dressings, and making sure meats and fish are fresh—not frozen or processed. For the traveler, most airlines will provide a low-sodium meal if notified in advance, and hotels will often equip a room with a small refrigerator for stocking low-sodium items.

Fast food restaurants are, generally speaking, a no man's land in the battle to reduce sodium consumption. According to the figures supplied by the chains, the sodium contents of the items run: 393 mg for a Burger Chef hamburger, 960 for a Big Mac and 2,285 for a Kentucky Fried Chicken Original Recipe dinner. A hamburger, french fries and a chocolate shake will total 965 mg of sodium, according to *The Dell Color-Coded Low-Salt-Living Guide*.

The American Council on Science and Health, which describes itself as an "independent educational association promoting scientifically balanced evaluations of food, chemicals, the environment, and human health," recently published a booklet called *Fast Food and the American Diet*. The booklet includes this advice:

"Individuals who are under a physician's orders to reduce their sodium intake (common advice to people who have high blood pressure) should be aware that many fast foods are relatively high in sodium due to their high content of salt (sodium chloride). It may be impossible to fit some menu items into sodium-restricted diets. . . .

"Condiments such as pickles, catsup and mustard also contain substantial amounts of sodium. Consumers who add salt to fast food items before eating further increase the food's sodium content."

However, there are signs of hope for those people who love fast foods but need to know sodium content. Arby's restaurants are providing nutrition composition information, including sodium quantities, for foods listed on their menus. McDonald's has also done pilot tests on a nutrition listing program.

In commenting to *FDA Consumer* about living without added salt, James Beard said the only taste he missed was bread made with salt. But the authors of the various salt-free cookbooks offer a variety of salt-free breads, ranging from apple juice rye bread (1 mg sodium) in *The Dieter's Gourmet Cookbook* to Claiborne's hamburger buns to the low-sodium white bread in *Cooking Without A Grain of Salt*. The heart association's saltless cookbook lists two dozen items under the heading of "breads."

Some say it's impossible to eat a hard boiled egg without putting salt on it. But boiled, poached or fried eggs can be seasoned delightfully with the pepper shaker. Other egg dishes can be seasoned with paprika, tarragon, savory and chives, according to the book *Salt-Free Cooking With Herbs and Spices*. But eggs in themselves are not exactly low-sodium food. One egg contains about 60 mg of sodium, 51 of that in the whites.

A scientific study done for FDA on sodium concluded that the aggregate consumption of sodium should be lowered. In other words, all of us should cut down on the amount we use. Recent scientific evidence indicates that people with slightly raised blood pressure will usually benefit from sodium-restricted diets, as do those who take prescribed drugs for their hypertension. Less sodium in the diet tends to make the drugs more effective and results in fewer and less severe side effects.

Diseases of the heart are the nation's No. 1 killer. Hypertension is often an accessory in those deaths. So, even though that recipe may call for just a pinch of salt, remember that a few pinches can add up to a considerable ouch.

Roger W. Miller is editor of FDA Consumer.

Death Helped Write The Biologics Law

Diphtheria A
Purified Glob
Super-Concentrated
5000 UNITS
130

by Ramunas A. Kondratas

It was nearly 80 years ago, on July 1, 1902, that President Theodore Roosevelt signed into law "an act to regulate the sale of viruses, serums, toxins, and analogous products in the District of Columbia, to regulate interstate traffic in said articles, and for other purposes." The new federal law attempted to control the interstate and foreign sale of a specific class of drugs in the United States preceding by four years the first Food and Drugs Act.

Identification of microbes as causes of disease, discovery of sources of infection and understanding of the modes of transmission had made it possible for physicians and public health workers during the latter half of the 19th century to develop more specific methods of prevention. Serum therapy and the newly emerging science of immunology were important milestones in developing specific remedies—antitoxins and vaccines—for mass prevention and treatment of many epidemic, communicable diseases that scourged mankind at the turn of the century. Until then vaccination was successful only against smallpox and only a very few specific remedies were known, such as quinine for malaria and mercury compounds for syphilis.

Some of the first specific remedies devised by man came out of Koch's laboratory in Berlin in 1890 where it was found that animals injected with diphtheria and tetanus toxins produced antitoxins that provided immunity to animals or humans inoculated with them. Of more importance, this serum could actually cure the diseases. Large scale production of diphtheria antitoxin began after Emile Roux reported in 1894 his successful effort at producing antitoxins from horses. Roux's study of serum therapy was based on four years of laboratory experiments and the treatment of hundreds of cases of diphtheria. Under serum therapy, mortality from diphtheria in Paris hospitals was

.......,189
htheria-Antit
10 Cubic Centimeters
strength 1 to
at the Hygienic
Marine-Hospital

reduced from 52 percent to less than 25 percent. The clinical success of diphtheria antitoxin in Europe and later in the United States acted as a powerful stimulus for the development of pharmaceutical firms and public health laboratories.

By the spring of 1895, the first samples of diphtheria antitoxin had been produced and tested in New York City and Washington, D.C. The H. K. Mulford Co. of Philadelphia was the first pharmaceutical firm in the United States to manufacture the antitoxin.

Serum therapy opened a broad new field in preventive medicine, but at first there were some serious pitfalls. Lacking were a good working knowledge of bacteriology and the sterile technique for successful production of serums and vaccines. Proper dosage forms and sterile containers had to be designed. Laboratory equipment had to be manufactured or imported. Proper refrigeration was a requisite and stables and animal shelters needed to be kept absolutely clean with the animals free from disease and infection. Most important, standards of purity and potency had to be established and enforced. All had to be done at a reasonable cost and at a time when the science of bacteriology was still in its infancy on American soil.

Diphtheria antitoxin was a powerful new weapon for the physician, but without proper standards and safeguards it could have been misused and could have brought harm to the public and the medical profession. The failure of tuberculin developed by Koch a few years earlier was still fresh in the minds of many physicians and they viewed with skepticism the glowing reports about diphtheria antitoxin. In Germany competition developed between pharmaceutical manufacturers in the production of serum, with firms boasting of the strength of their serums. Joseph Kinyoun, director of the U.S. Hygienic Laboratory, speculated about what could happen in the United States without government supervision. He wrote:

"... Many persons will, during the ensuing year, commence to prepare the serum as a business enterprise, and there will, without doubt, be many worthless articles called antitoxin thrown upon the market. All the serum for sale should be made and tested by competent persons. Testing, in fact, should be done by disinterested parties. ..."

Indeed, the Dec. 22, 1894, issue of the *Journal of the American Medical Association* cautioned the medical profession that one or more fraudulent antitoxins for diphtheria were already on the market and that only a few small packages received from Germany were known to be reliable and guaranteed. A few weeks earlier the New York City Board of Health had issued a circular urging that steps be taken to supervise the sale of diphtheria antitoxin in the city by inspecting and scientifically examining the various preparations of antitoxin offered for sale to verify their strength and purity. The board warned that it would institute criminal proceedings in instances of fraud or the marketing of inferior preparations.

In the medical literature and records of the time several major arguments emerged for regulating biologicals. The purity of serums, toxins, antitoxins and analogous products was considered far more important than that of ordinary drugs because biologicals were normally introduced directly into the circulatory system instead of the digestive tract and could not be withdrawn, once administered. Biologicals were most effectively given in full doses in the early stages of a disease, and if these were worthless or below strength, the loss of time could cost the life of the patient.

M 478-82
Rabies Vaccine
PASTEUR METHOD
For Human Use
H. K. MULFORD CO.,
U. S. Gov. License No.

Other arguments dealt with inspection. It was noted that there could be no assurance of purity if control was limited to inspection and tests of the final product, as preparations differed between one animal and another. Efforts therefore had to be directed toward licensing the establishments where these products were manufactured.

Before the 1902 act, "any kind of a stable, a little technical skill, and a fair amount of nerve" were all that was needed to produce and sell biologicals, according to a U.S. Senate report. Furthermore, since most of the biologicals were sold in states other than the ones in which they were produced, individual states were powerless to protect themselves against impure and impotent materials without federal supervision.

It took a tragedy to mobilize popular and professional opinion and induce the legislators to act. This event occurred in the fall of 1901.

On Oct. 26, 5-year-old Veronica O'Neill died in the St. Louis city hospital from tetanus. She had been admitted nine days earlier and was given two shots of diphtheria antitoxin. Her physician notified the city health department that her death was undoubtedly caused by tetanus-infected antitoxin. The department immediately stopped further distribution of the antitoxin and asked for an investigation. On Oct. 30 it was reported that a horse that over the past three years had furnished over 30 quarts of diphtheria antitoxin had come down with tetanus and had been killed. Two flasks of serum from the dead horse were dumped into the laboratory sink. The next day the *St. Louis Globe Democrat* reported the deaths of four more children, describing them as "antitoxin victims."

More investigations followed. In the

meantime, the number of children's deaths from tetanus rose to 13. On Feb. 12, 1902, a special investigating committee recommended that a consulting bacteriologist who had supervised the antitoxin production and distribution be dismissed and that the city get out of the antitoxin manufacturing business. The city health commissioner complied.

The St. Louis incident was widely reported in the nation's press and some physicians were afraid it would be used by opponents of serum therapy in general. An editorial in *JAMA* warned that "anti-vaccinationists, antivivisectionists, 'Christian Scientists,' and crotchety persons in general" would use this incident for "evil purposes." It became clear that action was needed to preserve the confidence of the medical profession and the public in biologicals.

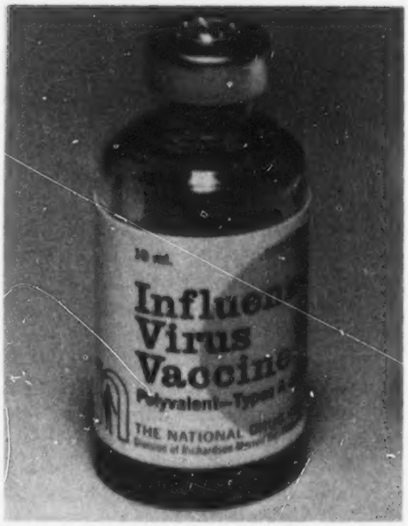
The Medical Society of the District of Columbia took the initiative and in spring 1902 proposed legislation to regulate the sale of biologicals. The District medical society had consulted with the U.S. Public Health Service, which had been considering drafting similar legislation; but the congressional committees did not ask for comments from the Public Health Service nor its parent organization at the time, the Treasury Department. Thus, without much comment or discussion, and without any publicity, the act was signed into law by the president on July 1. This stands in great contrast to the heated debates and deluge of publicity attendant to the enactment of the first Food and Drugs Act four years later.

The 1902 act set up a board composed of the surgeon general of the Army, the surgeon general of the Navy, and the supervising surgeon general of the Marine Hospital Service. The board was given authority, with Treasury Department concurrence, to promulgate regulations for licensing companies engaged in the sale and preparation of viruses, serums, toxins, antitoxins and analogous products in interstate or foreign commerce. The act made it unlawful to transport or sell preparations not prepared at a licensed establishment, and not carrying identification of the manufacturer as well as a date beyond which the contents could not be expected to yield "their specific results." The Public Health Service was given power to inspect the premises of any establishment manufacturing these products. The penalty for violations was a fine of up to $500 or a maximum of a year's imprisonment or both.

There were European precedents for federal regulation. As early as 1895, laws regulating the manufacture, sale and distribution of biologicals had been enacted by the governments of France, Germany, Italy and Russia. They dealt with the licensing and inspection of products by government approved laboratories, proper labeling and the accreditation of manufacturing places.

The first regulations under the new act were promulgated Feb. 21, 1903, and became effective six months later. They dealt with licenses and inspections. Before a license was granted a medical officer from the Public Health Service would make an unannounced visit to the manufacturing establishment and inspect the sanitary condition of the physical plant and the methods of preparing, storing and dispensing the products. His report was sent to the sanitary board of the service, which would make recommendations to the surgeon general and finally to the Secretary of the Treasury for action.

Licenses were issued for a year and could not be re-issued without reinspection. Licenses could be suspended for 30 days for faulty methods of preparation, faulty construction or administration of the establishments, for impurities, or for lack of potency of products as demonstrated by laboratory examination. If the faults were not corrected within 60 days, the license could be revoked. By 1904 a total of 13 establishments had been inspected and licensed, mostly for the sale of smallpox vaccine and diphtheria antitoxin. Parke-Davis and Co. received the first license and H. K. Mulford (now part of Merck Sharp & Dohme) the second. By 1921, a total of 41 establishments had been licensed for the interstate sale of 102 biologicals.



The regulations were strictly enforced. Some laboratories were refused a license or their licenses were suspended. Others simply closed down because they couldn't meet the standards. Marked improvement was shown in the quality of the products sold on the open market. Much original scientific work was done in the Hygienic Laboratory to establish the American standard of potency for diphtheria antitoxin and later for other vaccines. Products that did not meet these standards were taken off the market.

The Biologics Control Act of 1902 restored public and professional confidence in biological products by establishing and vigorously enforcing strict standards of purity and potency. It improved the quality of products on the market. It stimulated original research in government and private laboratories. On a more subjective level, it helped develop a relationship of mutual respect and cooperation between the federal government and the pharmaceutical industry. It set the tone for future drug regulation.

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The Notebook

The Notebook: a potpourri of items of interest to consumers, gathered from FDA press releases, other news sources, and the Federal Register *(designated FR with date of publication). The* Federal Register *is available in many large public libraries.*

■ **Victims of arthritis** will spend $2 billion on drugs and devices in 1990 according to a medical market report by Frost & Sullivan Inc., an international business research firm. Of this amount $1.3 billion will be spent on prescription drugs, up from $660 million in 1980, while OTC drug sales are predicted to go down to $400 million from a 1980 sales figure of $470 million. Devices will double in sales, from $120 million in 1980 to $240 million in 1990, according to the report.

■ Only 17 percent of the adult population asks physicians to prescribe **generic drugs** and only 20 percent asks pharmacists to fill prescriptions generically, according to a recent report from Arthur D. Little Inc. of Cambridge, Mass. Based on a July 1981 survey of 1,009 people by Opinion Research Corp., the report notes that the people most likely to ask for generic products were those with the most education and highest incomes and those in professional, managerial or owner occupations.

■ **Worldwide sales** of pharmaceutical products in 1981 were estimated at $76.28 billion, according to IMS-World. Estimates for 1980 were $76.02 billion, a 13.4 percent gain over 1979.

■ Department of Labor's Occupational Safety and Health Administration is taking a new look at its standards regulating employee exposure to **ethylene oxide** (EtO) in light of new information on possible health hazards of the gas. EtO is used in making antifreeze and heavy duty laundry detergents and is a sterilizing and fumigating agent used in hospitals, medical product and cosmetic manufacturing, in the food industry, beekeeping and dairy packaging (FR Jan. 26).

■ What manufacturers must do if they have to recall **defective infant formula** has been spelled out in a proposed FDA regulation. The rule would require a written evaluation of the health hazard, development of a recall strategy, prompt notification of FDA and progress reports every 14 days. The rule, mandated by the Infant Formula Act of 1980, will become effective 60 days after a final version is published (FR Jan. 15).

■ **Selenium sulfide** and **Selsun,** an anti-dandruff shampoo containing selenium, didn't cause cancer when applied to the skin of mice, but did prove carcinogenic in male and female rats and female mice when administered directly into the stomach. These were the findings of three long-term studies done by the National Toxicology Program and the National Cancer Institute. Results of the studies are available from the Office of Cancer Communications, NCI, Bethesda, Md. 20204 (FR Feb. 5).

■ Labels on **Meadow Fresh imitation dairy products** once claimed the products were nutritionally equal or superior to milk and contained no cholesterol. But those labels have been revised to meet FDA regulations. Among other things, foods that are a substitute and resemble another food but are nutritionally inferior must bear the word "imitation" prominently on the label. Several state agencies, including the Utah Department of Agriculture, accepted the revised labeling but say they do not endorse the products and that they should not be promoted and sold to child care centers, nursing homes and similar institutions. Meadow Fresh products are manufactured by Dairy Monitoring of America, Logan, Utah, and are distributed by Meadow Fresh Farms, Salt Lake City, via "pyramid" marketing.

■ A revised **drug experience reporting** form, now available from FDA's Bureau of Drugs, makes reports of adverse drug reactions more useful for analysis by adding information to help clarify the seriousness of the drug reaction and to determine if a cause and effect relationship exists (FR Jan. 22).

■ A grand total of 519 **medical devices** were classified by FDA for regulatory purposes during the first two months of 1982. The products, ranging from artificial body parts to surgical lasers, clinical testing materials and medical dressings were rated either class I (general controls), class II (performance standards) or class III (premarket approval). Here's a rundown on these latest device classifications. General and plastic surgery devices: I - 23, II - 24, III - 6, both II and III - 1 (FR Jan. 19); ear, nose and throat devices: I - 10, II - 47, III - 10 (FR Jan. 22); ophthalmic devices: I - 45, II - 51, III - 4, both I and II - 19 (FR Jan. 26); radiology devices: I - 7, II - 64, both II and III - 1 and I, II or III - 1 (FR Jan. 29); and clinical chemistry and clinical toxicology devices: I - 31 and II - 175 (FR Feb. 2).

Investigators' Reports

Unwelcome Ingredient

A can of wax beans contained an unpleasant surprise for a consumer in Augusta, Maine—a dead mouse. The consumer complained to the **Maine Department of Agriculture,** FDA became involved, and when the dust settled more than 6,400 cans of wax beans had been buried in the Augusta city dump.

When the State of Maine was presented with a can of beans in which the consumer had found a large foreign object, it asked a contract laboratory to do an analysis. The object turned out to be a mouse that had apparently been cooked with the beans.

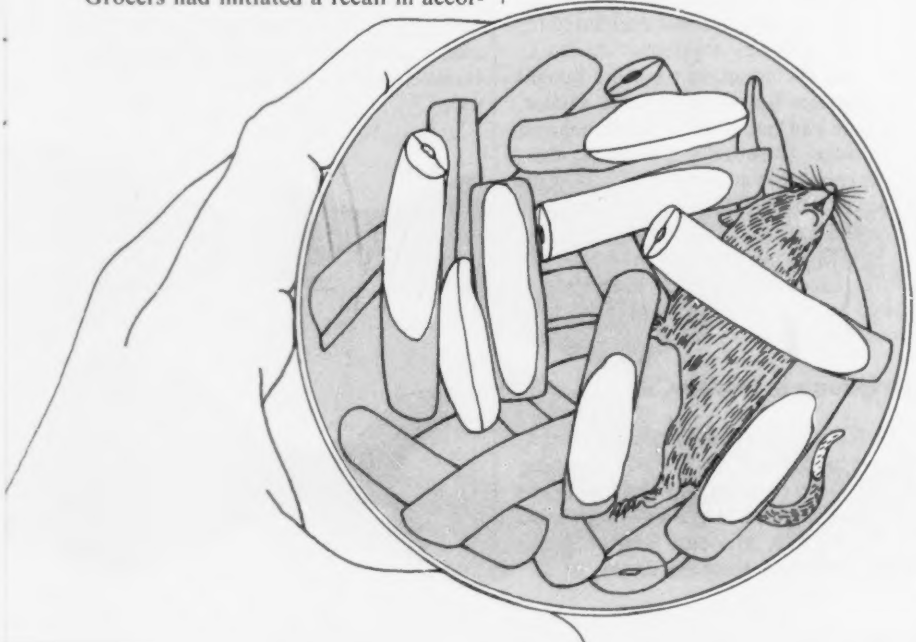
After the state notified FDA's **Augusta resident post** of the findings, an agency investigator visited the product distributor, Associated Grocers of Maine Inc. He took 48 sample cans of wax beans marked with the same production code as the one with the mouse. Analysis of the samples at the Boston district laboratory subsequently isolated rodent hairs in 21 of the 48 cans.

Armed with these findings, the state quickly placed an embargo on the entire code lot of wax beans and other codes packed in the same cases. The embargo included beans being returned to the distributor from 323 member retail stores located in Maine. Associated Grocers had initiated a recall in accordance with company policy.

The manufacturer of the beans, C-B Foods, Division of Curtice Burns Inc., of Rochester, N.Y., also was notified. The company replied that it considered the problem to be an isolated incident since its own analysis of beans in stock disclosed no problem, and it believed no further action was needed. FDA then recommended and received approval for seizure of the entire lot of Generic Cut Wax Beans under embargo in the Associated Grocers warehouse.

When notified by the United States attorney of the pending seizure, the manufacturer and distributor agreed to destruction of the lot. While an FDA investigator and the warehouse superintendent of Associated Grocers watched, 267 cases of beans containing 24 cans each were crushed and buried in the Augusta city dump. Their value was estimated by the manufacturer at approximately $1,468.

FDA had one final job to do. An investigator from the **Buffalo district** office inspected the C-B Foods plant in Alton, N.Y., that had processed and canned the wax beans. A three-day inspection revealed no conditions requiring further legal or administrative action by FDA; however, the company made some changes in its processing operations to reduce the possibility of similar problems with its canned products in the future.



Lost Appetite Solved

Some dairy farmers in eastern Canada, puzzled that their cattle were reluctant to eat and that milk production was down, asked advice from government farm experts. The experts decided that the magnesium oxide supplement sprinkled on the feed didn't look right, and probably didn't taste right to the cattle. It should have been creamy white; instead it was dark gray. Besides that, the label on the bags did not give the percentage of analysis (how much magnesium) as required by regulations.

The labels showed that the bags had been shipped by the Westmin Co. of Quincy, Ill. Canadian officials told FDA's **Chicago district** office about the problem, and FDA's **Springfield (Ill.) resident post** was asked to look into it.

The resident post investigators found that Westmin was hauling discarded fire brick from steel mills in Harbor, Ind., to Solomon Grind-Chem Service right there in Springfield. Solomon would grind up the bricks, then bag, store and ship the powder labeled as magnesium oxide to various distributors in several midwest states and Canada. The oxide was then sold to farmers as a feed supplement.

Samples of Solomon's bagged oxide were sent by investigators to FDA's laboratory in Cincinnati for analysis. The lab found that the percentage of magnesium oxide was substandard and varied from bag to bag. Toxic heavy metals were also found in the samples. In addition, there was an amber oily residue that the lab could not identify. The residue was sent to FDA's Detroit laboratory for further analysis. The Detroit laboratory separated the residue into five compounds, each of which was found to be an organic, cancer-causing substance. These findings of heavy metals and carcinogens made the ground-up bricks unsuitable as an animal feed supplement, because animals eating the feed would be harmed, and humans who consumed the milk or meat of the animals could also be affected.

The fire brick, made with special clays and a high metallic content, had been used to line the steel mill furnaces. The white-hot temperatures in these furnaces normally vaporize the organic (oily) compounds that FDA's laboratories found. But some bricks, because they were damaged or defective, had not been used in the furnaces and so had not been exposed to the intense heat. They were tossed into the discard pile, then hauled away by Westmin along with the used brick. The carcinogens in the oxide grind came from these unused bricks.

Neither Westmin nor Solomon would, at first, cooperate with FDA by providing shipping records to help locate interstate shipments. But by checking with contract truckers and other sources, FDA identified purchasers of the supplement in several states. Samples of the bagged supplement in those shipments showed the same general mix of magnesium, heavy metals and carcinogens.

Informed that the feed supplement violated the Food, Drug, and Cosmetic Act, Westmin recalled all outstanding shipments, totaling some two million pounds, for possible reconditioning as an industrial powder.

2-Legged vs. 4-Legged

Spotting insects is part of the routine in an FDA warehouse inspection and is one of the reasons FDA exists. Working their way through the stored goods, FDA investigators stay alert for signs of six-legged and eight-or-more-legged creatures, for beetle droppings, and other evidences of entomological infestation of food or food packaging.

But an investigator from FDA's **Atlanta district** found something four-legged while inspecting a Revco Co. warehouse in North Augusta, S.C. The Georgia Department of Agriculture had told the district staff that chocolate candy containing insect fragments had been showing up in Revco drug stores in the Atlanta area. An FDA investigator was dispatched to check out the warehouse from where the candy shipments had been stored.

The investigator's search through boxes of chocolate bars and grape candy failed to reveal a significant insect problem, but there was a four-legged one: Mice were found in the food storage area along with three rodent nests (two with baby mice). The problem was serious enough to warrant seizure and destruction of approximately 221 cases of candy, valued at $5,599.

Sardine Saga

During eviction proceedings against a tenant of a Brooklyn warehouse, the New York City marshal's office found about 300 cases of canned sardines in the building's basement. Signs posted over the merchandise read, "Poison. Do Not Touch."

An investigator from the FDA's **New York district** office took 50 sample cans of sardines from the warehouse basement and turned them over to the New York regional laboratory for analysis. The findings: 12 of the 50 cans, or nearly 25 percent, were swollen, and some improperly formed can seams were evident. No microorganisms were found; the swelling was due to overfilling (as much as 20 percent) and to the presence of carbon dioxide and hydrogen gases.

Back at the warehouse, the landlord who had instituted the eviction said he was unwilling to pay for disposing of the sardines—that it was the original purchaser's or FDA's problem. The New York district tracked down the attorney representing the owner of the merchandise, a clothing textile remnant salvage operator who had decided to try food salvaging as a sideline. At least, that was his intention when he bought the sardines four or five years earlier, but they had remained in the warehouse ever since. Eventually he noticed that some cans were swelling and posted the "poison" signs, apparently deciding to abandon his salvaging enterprise.

At FDA's request the State of New York placed the sardines under embargo to prevent movement until they were destroyed.

Dripdown in Dodge City

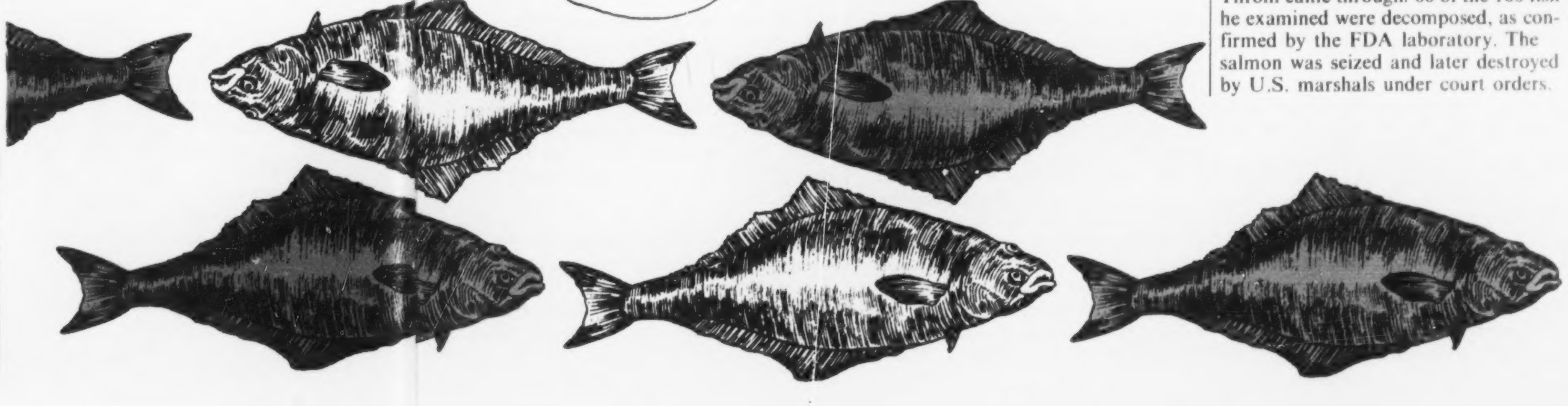
A Kansas meat packer has decided that it will never again store anything on the large concrete slab that covers its million-gallon underground water tank.

The packer, Missouri Beef of Dodge City, had been stacking drums of industrial chemicals and other supplies on the flat concrete surface. But a 55-gallon drum of hide-curing compound (tetrachloroethylene and orthodichlorobenzene) broke open and leaked into the water supply below. The incident happened on the night shift at the plant. It was not noticed until the water, used to process the company's various products, had contaminated some 3,000 animal carcasses and several thousand pounds of animal by-products.

The **U.S. Department of Agriculture** shut down the plant and ordered the beef carcasses held to determine the extent of contamination. FDA's concern was possible contamination of tallow, bone meal and blood meal that the plant normally converts for animal feed.

Samples of these by-products were collected by FDA's **Kansas City district** office and flown to agency laboratories in Washington, D.C. There, Bureau of Foods scientists worked through the weekend doing analyses. The scientists found high levels of the chemicals in the tallow, predictable because the spilled chemicals are defatting agents that would be drawn to fat and tallow. The other by-products were found acceptable.

USDA released the beef carcasses after organs and trimmings that had high chemical levels were removed and buried in a landfill. USDA also required that fat be trimmed from the carcasses. The tallow that FDA found contaminated was diverted to industrial use.



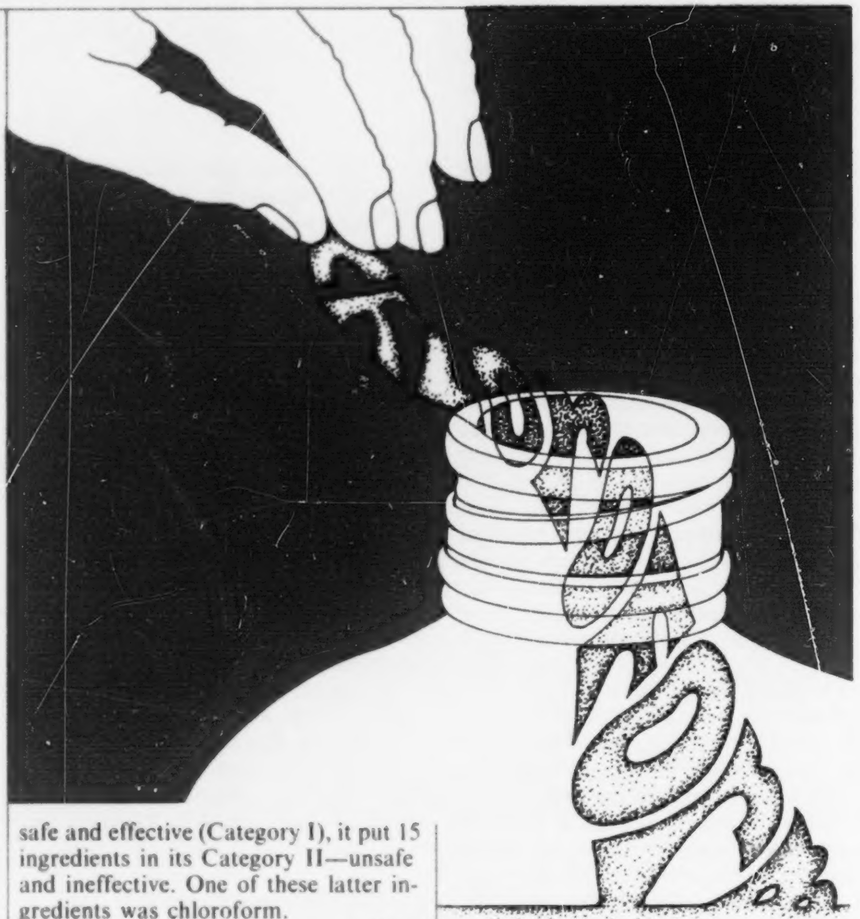
This Nose Knows

The fishing boat off the Alaskan coast may have taken a larger catch than its freezing capacity could handle, or the fish may not have been properly iced when they were dumped into the hold. Whatever the reason, some 24 tons of frozen halibut that FDA found in commercial cold storage in Mount Vernon, Wash., showed signs of decomposition that would keep them from being marketed.

An inspector from the **Seattle district** office was checking the cold storage plant when he came across the suspect halibut. He called in the district organoleptic specialist, Richard Throm, an expert in detecting decomposition in fish by using his trained sense of smell.

Throm drilled into the now hard-frozen halibut, sniffed the area warmed by the drilling action, and found there was decomposition. He did this with 65 fish in the storage plant, and found that 28 were decomposed. His findings were confirmed by later analysis in the district laboratory. The entire lot, valued at $83,000 wholesale, was seized by a U.S. marshal under court order. With no chance of using the fish for human food, the owners separated the decomposed from the acceptable halibut under FDA supervision. The 30 percent of the lot that was decomposed was destroyed.

Throm was also asked by a district investigator to check some frozen salmon the investigator was suspicious about in the Bellingham Cold Storage Co. at Bellingham, Wash. Again Throm came through: 60 of the 100 fish he examined were decomposed, as confirmed by the FDA laboratory. The salmon was seized and later destroyed by U.S. marshals under court orders.



Whey-out Labeling

FDA doesn't kid around when it comes to recipes for kids.

Coleco Industries Inc., Rochester, N.Y., is routinely inspected by FDA because it repacks the various cake mixes that come with its toy ovens, from a bulk shipment made by a cake mix manufacturer. The company got a letter from the **Buffalo district** office recently when it failed to notice that the manufacturer had changed the ingredients.

During an inspection of the company an FDA investigator noticed that the ingredients list on a 1-ounce packet of pie crust mix failed to declare the presence of the dried whey that was in the bulk supply mix list. The investigator reasoned the error might mislead parents of children with allergies to milk protein, since dried whey is a portion of milk separated during processing, so he collected a sample of the product.

After an FDA laboratory found the product contained 2 percent to 4 percent whey, the district office sent a letter to the company reporting the deviation. As a result, Coleco has changed its labels.

Cough Syrup Embargoed

When two brands of non-prescription cough syrup containing chloroform were manufactured—sometime before 1976—they could be shipped legally in interstate commerce. But in 1981 a shipment of the same products was embargoed by the **New Jersey Department of Health** because interstate shipment of the cough medicine was illegal.

The status of the expectorant products, manufactured by a New York City company, was changed in 1976 as part of FDA's review of non-prescription drug ingredients for safety and effectiveness. This review was initiated by FDA in 1972 and conducted by 17 advisory panels, whose members were chosen by FDA. One of the first panels to conclude its studies was the panel on cough, cold and related products and, although it found many commonly used ingredients to be both safe and effective (Category I), it put 15 ingredients in its Category II—unsafe and ineffective. One of these latter ingredients was chloroform.

Ingredients placed in Category II by this panel undergo review by FDA; and the agency, after considering the panel's recommendations and other information, may issue regulations in the form of a monograph approving ingredients considered safe and effective and prohibiting the use of those not so considered. FDA's final monographs on the dozens of drugs being reviewed by the panels are expected to be published over the next few years after the agency has considered all the information available. Final regulations have not yet been issued on the cough and cold panel's 1976 study report (although some manufacturers have already removed Category II ingredients from their products).

But chloroform was a special case, and the panel had proposed immediate action. Studies had shown that chloroform in cough medicine could cause tumors in mice and rats and therefore might be carcinogenic in humans, as well. For that reason, FDA banned cough products containing chloroform after receiving the panel's report. However, so as not to cause economic hardship to drug manufacturers, the agency said that products already manufactured and on the market in 1976 could be sold until stocks were depleted—provided that the products were not shipped out of the state where they were located at the time the regulation went into effect.

If the cough medicine manufactured by the New York firm—Pisos brand and Pinex brand—had remained in New York, it would have remained a legal product after 1976. However, when the drugs crossed state lines from New York to New Jersey, FDA regulations were violated. The products' travels were traced by FDA's **New York district** after the district was called by an employee at a salvage distributor who had noticed that chloroform was listed as an ingredient on the recently purchased cough syrup. The major portion of the lot, still located in New Jersey, was embargoed by the New Jersey health department at the request of the district.

Seizures and Postal Service Cases

FILED SEIZURE ACTIONS

charge violations of the Federal Food, Drug, and Cosmetic Act and are initiated based upon FDA recommendations. A seizure action is commenced by the filing in the U.S. district court where the goods are located. A U.S. marshal is then directed by the court to take possession of the goods, removing the product from commerce, until the matter is resolved.

A total of 16 actions to remove from the consumer market products charged to be violative was reported in January. These actions included 15 charges of food concerning contamination, spoilage and insanitary handling, and one charge concerning medical devices.

PRODUCT, DISTRICT & DATE FILED	FIRM & PLACE OF BUSINESS	CHARGES
	FOOD/Contamination, Spoilage, Insanitary Handling	
Beans, farina, chocolate drink mix, and corn flour/U.S. District Court for the District of Puerto Rico 12/3/81	Sucrs. de Esmoris & Co. Inc./Mayaguez, Puerto Rico	Products have been held under insanitary conditions.
Chili sauce and bean sauces/U.S. District Court for the Northern District of Illinois 11/25/81	Shipped from San Francisco, Calif.	Products contain mold; contained in leaking jars.
Garlic bulbs, dried/U.S. District Court for the District of Puerto Rico 9/22/81	Shipped from outside Puerto Rico	Product contains insect filth—decomposed garlic bulbs.
Halibut, frozen, dressed and headed/U.S. District Court for the Western District of Washington 9/11/81	Sitka Sound Seafoods/Sitka, Alaska	Product contains decomposed fish.
Macaroni products/U.S. District Court for the Western District of New York 1/18/82	Olindo Imported Foods Inc./Rochester, N.Y.	Products have been held under insanitary conditions.
Macaroni products and other foodstocks/U.S. District Court for the Southern District of Texas 12/3/81	Antone's Imports/Houston, Texas	Some products are contaminated with insect filth; all of the products have been held under insanitary conditions.
Pancake mix/U.S. District Court for the District of Puerto Rico 11/30/81	Shipped from New Orleans, La.	Product contains insect filth.
Pancake and waffle mix/U.S. District Court for the District of Puerto Rico 10/20/81	Shipped from New Orleans, La.	Product contains insect filth.
Papaya chunks, canned/U.S. District Court for the District of Puerto Rico 10/23/81	Shipped from San Paulo, Brazil	Product is contained in swollen and leaking cans.
Rice, cheese, macaroni products and other foodstocks/U.S. District Court for the Western District of Washington 10/13/81	Pacific Food Importers/Seattle, Wash.	Some products contained rodent or insect filth; all products had been held under insanitary conditions.
Rice flour/U.S. District Court for the Eastern District of Missouri 1/12/82	Shipped from Memphis, Tenn.	Product was held under insanitary conditions.
Rice and sweet sauce/U.S. District Court for the Western District of Missouri 11/24/81	King's Trading Inc./Kansas City, Mo.	Rice is contaminated with rodent filth, and both products were held under insanitary conditions.
Salmon, dressed, frozen/U.S. District Court for the Western District of Washington 11/17/81	Can-Inter-Foods Ltd./Delta, Canada	Product contains decomposed salmon.
Sesame seeds and sesame seed syrup/U.S. District Court for the District of Puerto Rico 10/16/81	Tropical Fruit Products Co./San German, Puerto Rico	The sesame seeds contained rodent filth and had been held under insanitary conditions, and the syrup had been prepared under insanitary conditions.

PRODUCT, DISTRICT & DATE FILED	FIRM & PLACE OF BUSINESS	CHARGES
Strawberries with sugar, frozen/U.S. District Court for the Western District of Washington 9/25/81	Valley Packers Inc./Puyallup, Wash.	Product contains decomposed strawberries.
	MEDICAL DEVICE	
DuraSoft 2 (phemfilcon A) hydrophilic bifocal contact lenses/U.S. District Court for the Northern District of Illinois 1/4/82	Wesley-Jessen Inc., Division of Schering Corp./Chicago, Ill.	Products are class III devices and fail to have in effect either an approved application for premarket approval or an exemption for investigational use.

U.S. POSTAL SERVICE

actions taken in medical cases as authorized in the Mail Fraud Statute (18 U.S.C. 1341) and/or the False Representation Statute (39 U.S.C. 3005) as reported by the Chief Postal Inspector.

False Representation Orders Issued by Judicial Officer Under 39 U.S.C. 3005

October 6, 1981: Against **Cedar Hills Pharmacal,** RD 1, Box 128, Milroy, Pa. Satisfactory evidence was presented to the Postal Service that Cedar Hills Pharmacal and its agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising "Stimulants." These stimulants are being sold as look-alike narcotics.

October 6, 1981: Against **R&A Distributors,** P.O. Box 493, Springfield, Tenn. Satisfactory evidence was presented to the Postal Service that R&A Distributors and its representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising "Stimulants." These stimulants are being sold as look-alike narcotics.

October 27, 1981: Against **California Medical Research,** P.O. Box 4855, San Diego, Calif. Satisfactory evidence was presented to the Postal Service that California Medical Research and its agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "CMR Contour Creme," representing the ability to "take off bloaty cellulite and ugly inches without pills, shots, exercise or hunger."

October 28, 1981: Against **The House of Renee,** One Wolfs Lane, Pelham, N.Y. Satisfactory evidence was presented to the Postal Service that the House of Renee and its agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Gege Lotion." The ad states, in part, "at last your stretch mark problems gone for good! If you're ashamed of ugly stretch-marks, and really want to do something about them, then it's time you tried Gege Lotion!"

October 30, 1981: Against **The Health Energetic Co.,** 2600 E. Coast Highway, Corona Del Mar, Calif. Satisfactory evidence was presented to the Postal Service that The Health Energetic Co., and its representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "S-Energetic," representing the ability to "restore your vitality; improve your vigor; reduce breathlessness and fatigue; help combat skin disorders; improve physical appearance, scientifically increase energy levels."

November 4, 1981; Against **Starr Retailers,** P.O. Box 518, Milroy, Pa. Satisfactory evidence was presented to the Postal Service that Starr Retailers and its agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising "Stimulants." These stimulants are being sold as look-alike narcotics.

November 5, 1981: Against **Dalen Labs,** P.O. Box 118, Westmont, Ill. Satisfactory evidence was presented to the Postal Service that Dalen Labs and its representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Tropical Tan," representing the ability "to get a deep-dark brown tan."

November 5, 1981: Against **V.V.& L.,** RR 1, Box 312, Milroy, Pa. Satisfactory evidence was presented to the Postal Service that V.V.& L. and its agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising "Stimulants." These stimulants are being sold as look-alike narcotics.

November 30, 1981: Against **Doctor's Capsule Plan,** 1255 Post St., San Francisco, Calif. Satisfactory evidence was presented to the Postal Service that Doctor's Capsule Plan and its representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Doctor's Capsules," representing the ability to "lose the fat forever. Lose 10, 20, 30 . . . even 60 pounds or more—without time consuming exercise—without one moment of hunger!"

Complaints filed by Law Department Under 39 U.S.C. 3005 (False Representation)

October 14, 1981: **The Mail Order Discount Shopper,** Box CY 373/400 Commonwealth Ave., Boston, Mass. Advertising and sale through the mail of the product "The Boston Hair Life Program," representing the ability to "grow new hair . . . the belief that hair follicles are absolutely dead after five years of not growing hair has been disclaimed . . . the procedures utilized by the clinics came about as a result of an extensive scientific research project that demonstrated success in developing a method for stopping excessive hair loss and growing new hair."

October 16, 1981: **Maga Research, Ltd.,** P.O. Box 667, Lynbrook, N.Y. Advertising and sale through the mail of the product "Maga Technique Program." The ad states, in part, "new tests prove doctor's wonder enlargement technique can give any woman a dramatic new bustline in just one week! No surgery . . . no padding . . . no exercisers . . . no drugs. Yet many women see up to a 3 inch improvement in 7 days or less."

November 2, 1981: **That Special Look, Inc.,** P.O. Box 1490, Pompano Beach, Fla. Advertising and sale through the mail of the product "Sauna Suit," representing the ability to "turn leisure time into weight loss time, slims your waist, hips and thighs. No pills. No hunger! Works while you relax . . . best, most effective ways to shed unwanted pounds."

November 3, 1981: **Rockwell Scientific Industries,** 210 Fifth Ave., New York, N.Y. Advertising and sale through the mail of the product "Astro Triplex." The ad states, in part, "enlarge your bosom 3 full cup sizes in only 1 week!!!"

November 3, 1981: **Bradford Warner,** 521 Fifth Ave., New York, N.Y. Advertising and sale through the mail of the product "Living Fluids and Living Creme," representing the ability to "enlarge your bosom . . . be big busted beautiful in an era of small bosomed women . . . gain up to 6 inches and 3 cup sizes now!"

November 3, 1981: **Swedish Extract,** 175 Fifth Ave., New York, N.Y. Advertising and sale through the mail of the product "Big Bosom Creme." The ad states, in part, "increase your bosom . . . new Swedish discovery . . . adds inches while you sleep. Be the new sexy big size you want to be! Yes, help is finally here for small breasted women."

Notices of Judgment

NOTICES OF JUDGMENT on Seizure Actions

FOOD/Contamination, Spoilage, Insanitary Handling

Cocoa bean sweeps, at Philadelphia, E. Dist. Pa.

Charged 2-14-78: while held by Atlantic & Gulf Stevedores Inc., Philadelphia, Pa., the article contained insect filth and moldy cocoa beans; 402(a)(3) and (4). The article was claimed by the dealer who denied the charges and asserted that the article had been rebagged and prepared for export sale (no intention of selling or offering for sale in domestic commerce).

The parties served written interrogatories on each other. Thereafter, the action came on for trial, on the issue of whether the claimant could be allowed to export the beans, having previously stipulated that the cocoa beans were contaminated. The court ruled in favor of the government, saying:

"First of all, within the meaning of 21 U.S.C., section 334, I find—because it is stipulated—that the article of food consisting of some 200-plus bags of cocoa beans which are at issue in this case are adulterated within the meaning of 21 U.S.C. section 342(a)(3) and that they are being held for sale after shipment in interstate commerce. . . . [A]dulteration and presence in interstate commerce having been stipulated—I have no alternative but to enter a decree of condemnation.

"Under these circumstances I find that the claimant has met neither the requirements of 21 U.S.C. section 334(d), nor 21 U.S.C. section 381(d), which are necessary in order for it to obtain the relief it seeks, i.e., permission to ship the goods to the Netherlands.

"First of all it is plain to me that the statute that applies to this case is 21 U.S.C. section 334(d) which in turn incorporates by reference the requirements of 21 U.S.C. section 381(d). I do not believe that 21 U.S.C. 381(d) can be applied in isolation in this case. Section 381(d) in isolation applies, as I see it, to goods produced here and intended for export, and the reference from the legislative history supplied by Mr. Ewing supports that contention. 21 U.S.C. section 334(d) coupled with section 381, which it incorporates by reference, fits glove-like into this situation, i.e., they deal with goods which were imported by design or accidently, perhaps here it was accidentally, got into commerce and were adulterated and then you want to ship them back for processing or simply for return. Section 334(d)(1) applies here, I so hold.

"I find that the claimant, A&G [Atlantic & Gulf Stevedore Inc.], who is the person seeking the release of the goods, has not met the requirements of either (a) or (d) of 21 U.S.C. section 334(d)(1).

"First of all, I find that the significant portion of the adulteration occurred after the article was imported, i.e., when the cocoa beans were swept up on the pier, allowed to accumulate and remain on the pier for a considerable period of time. I note in this regard that for quite some period of time the goods were flat on the pier and were not even raised on pallets where they would be free from damage by moisture and water.

"The evidence here supports my finding that the contamination by virtue of contact with dirt and grime on the pier and deterioration of the beans occurred in the year and a half period that they were left on the pier before delivery to Mr. Comly's warehouse.

"Secondly, I find that A&G had cause for believing that the goods were adulterated before they were released from Customs custody simply because in this case, as in every case, a certain number of beans will have mold (the Codex Alimentarius standard demonstrates that) but more to the point because there is a certain amount of sweeps which come out of every vessel which is discharged at A&G and at other terminals in Philadelphia. That is because the longshoreman's hooks will break the bags and some bags will not be tightly secured and there is always a certain amount of cocoa bean material which comes into contact with the pier.

"In any event, the claimant has not met the requirements of section 381(d). Although I am satisfied that the sweeps would accord to the specifications of the foreign purchaser, Mr. Tollig, of the Netherlands, the claimant has not established that shipment would not be in conflict with the laws of the Netherlands. Neither do I find section 381(a) which Mr. Thomas invoked to be applicable.

"I think it would be useful to state in some greater degree of particularity the facts about the cocoa beans themselves.

"I find they were collected over a period of one and a half years over some 16 separate shipments for which claimant Atlantic & Gulf Stevedores acted as consignee.

"I find that the solvent extraction process utilized by H. G. Tollig's company of Rotterdam, which is proposed to be applied to the cocoa bean sweepings in this case, would produce a commercially valuable product from which impurities had essentially been removed.

"I find a pharmaceutical quality product, including cocoa butter which could be applied to a variety of uses would emerge from such process.

"I find that the solvent extraction process is available in the Netherlands and several other companies in Western Europe but is not available in the United States.

"I find that there is no process available in the United States which could result in salvaging of these cocoa beans for any pharmaceutical use or any food use.

"I find that the mechanical processes which have been testified to would be unsatisfactory and would not be commercially applied.

"I further find the end product after the Tollig's refining would not endanger the health and safety of consumers either in the United States or abroad.

"Additionally, I find that the commercial value of the cocoa bean sweeps on the present market is approximately $25,000.

"For all of these reasons it is most unfortunate that the result in this case must be a decree of condemnation.

"As I read the facts of this case, which represent the result of common practice in the cocoa bean trade, it is almost never possible for cocoa bean sweeps to be shipped to Western Europe for reprocessing. That is because this case obviously represents the pattern in the industry. I think that that result is most unfortunate. When it becomes necessary to destroy products which have commercial value and which can be put to pharmaceutical use because of the cutoff of the law applied to a unique set of facts, economic waste occurs. Economic waste of this kind contributes to world inflation. I therefore urge FDA through the Office of Legal Counsel to consider legislation which might enable FDA under stringent conditions to permit the export of cocoa bean sweeps to plants which have the capacity to reprocess them into a pure and pharmaceutically useful state.

"I find no merit in the claimant's contention that the statute is void for vagueness. Although I have suggested that there might be some substantive due process problems with the unfortunate result which has occurred, a reading of the substantive due process cases suggest to me that it is plainly within the power of Congress to visit this result upon that very low member of the inanimate object order, the class of cocoa bean sweeps which have laid in the nether reaches of docks and wharves and piers for as long as a year and a half.

"Additionally, there is no evidence that the sweeps have a commercial value of zero if not shipped for reprocessing to the Netherlands. The claimant might have introduced evidence to that effect but it did not do so. It therefore may well be that some commercial value, whether for dog food or fertilizer, or something, may be realized from the product at issue.

"I have not made formal findings as to when the beans were imported but I accept the Government's position that they are not imported until they enter the territorial boundary of the port of entry. Even if I were to accept the claimant' position it would not change my conclusion. I think that it is a fair statement that the goods do not clear Customs custody until they arrive at the port. Nor are they released until formal entry documents are presented, processed and approved. However, even if I were to accept the claimant's view, that would not change my conclusion.

"The foregoing constitutes my findings of fact and conclusions of law pursuant to Federal Rule of Civil Procedure 52(a)."

The claimant filed an appeal, which was dismissed upon motion of the claimant because the parties had stipulated to sign a consent decree. A consent decree of condemnation authorized release to the dealer for salvaging. However, FDA determined that the article could not be reconditioned for human food use. Subsequently, the government moved for a decree of destruction. The court denied the motion and ordered that FDA permit the claimant to remove the article to a New Jersey reconditioner under FDA supervision for visual inspection and division into one lot containing beans visibly moldy and containing insect filth (which was to be destroyed) and into a second lot determined to be free of visible insect filth or mold. The claimant was to submit proposals and plans for bringing the article into compliance.

The article was removed to the New Jersey reconditioner and the beans were examined and sorted into two lots. FDA objected to the sampling technique used to separate the article into two lots and advised that the article had additionally been contaminated with rodent filth, which (under FDA policy) mandated destruction.

A status conference was held to discuss the progress of the claimant's reconditioning attempts. The government set forth reconditioning procedures it deemed necessary to bring the article into compliance. The claimant did not avail itself of such opportunity, and instead the claimant decided that it wished to destroy the article. Accordingly, a supplemental consent decree ordered the article destroyed. (F.D.C. No. 61619; S. No. 78-143-457; N.J. No. 1)

Flour, at Metairie, E. Dist. La.

Charged 4-8-81: while held for sale, the article contained insect filth; 402(a)(3). Default decree ordered destruction. (F.D.C. No. 63435; S. No. 81-222-196; N.J. No. 2)

Flour, at Yauco, Dist. Puerto Rico.

Charged 9-21-81: while held by Borinquen Macaroni Corp., Yauco, Puerto Rico, the article contained rodent filth and had been held under insanitary conditions; 402(a)(3) and 402(a)(4). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63536; S. No. 81-274-818; N.J. No. 3)

Flours, two lots, at Buffalo, W. Dist. N.Y.

Charged 9-22-81: while held by Barry Food Products Inc., Buffalo, N.Y., the articles had been held under insanitary conditions; 402(a)(4). Default decree ordered destruction. (F.D.C. No. 63563; S. Nos. 81-284-890/1; N.J. No. 4)

Pork and Beans, canned, at Tulsa, N. Dist. Okla.

Charged 7-24-81: while held for sale, the article was held in swollen containers; 402(a)(3). Default decree ordered destruction. (F.D.C. No. 63520; S. No. 81-267-141; N.J. No. 5)

Muffin mix, beans, flour, and **other foodstocks,** at Baltimore, Dist. Md.

Charged 4-22-81: while held by Andrews Food Co. Inc., Baltimore, Md., some of the articles contained rodent filth; and all of the articles had been held under insanitary conditions; 402(a)(3) and (4). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63450; S. No. 81-240-541 et al.; N.J. 6)

Tarragon leaves, ground jalapeno, and **ground fenugreek,** at San Antonio, W. Dist. Texas.

Charged 3-29-81: while held for sale (by San Antonio Spice Co., San Antonio, Texas), the articles contained insects; 402(a)(3). Default decree ordered destruction. (F.D.C. No. 63395; S. No. 81-222-690; N.J. No. 7)

"Maple" syrup, at Raymondville, S. Dist. Texas.

Charged 3-20-81: when shipped by H.W. Pilgrim, DeKalb, Miss., the article, labeled in part "Savage's Maple Syrup . . . Packed For Savage Farms Inc. Raymondville, Texas," had had corn syrup subsituted for maple syrup—402(b)(2); the labeling was false and misleading in representing that the food consisted wholly of maple syrup—403(a)(1); and the article failed to conform to the definition and standard of identity for maple syrup because the article was made with syrup from a source other than maple trees—403(g)(1). Consent decree of condemnation ordered constructive destruction by delivery to a suitable charitable institution for use only and not for resale. (F.D.C. No. 63328; S. No. 81-223-160; N.J. No. 8)

Potato-cheese pierogies (dumplings), sauerkraut-potato pierogies, and **potato pierogies,** at Hellertown, E. Dist. Pa.

Charged 11-1-79: while held by Hanka Foods Inc., Hellertown, Pa., who had manufactured the articles using interstate potato flakes, the articles' labels contained the false and misleading claims "Vitamin Enriched" and "No Preservatives Added," when the articles did not contain a significant amount of vitamin enrichment and did contain the added chemical preservative calcium propionate—403(a)(1); the articles' labeling lacked the common or usual name of each ingredient as required by regulations (e.g., lacked calcium propionate declaration and, for sauerkraut-potato pierogies only, lacked listing of ingredients in descending order of ingredient predominance)—403(i)(2); the articles' label lacked statements declaring the chemical preservative calcium propionate—403(k); and the articles were also in violation of the Fair Packaging and Labeling Act, since the quantity of contents statements were in too small type size and (potato pierogies only) the quantity of contents statement was not within the bottom 30 percent of the principal display panel area—15 U.S.C. 1453(a)(2) and 1453(a)(3)(C).

The articles were claimed by the manufacturer. A consent decree authorized release to the claimant for relabeling. Subsequently a question as to the whereabouts of the goods arose; and since no definitive explanation was provided to the government, the government moved for an order to take inventory of the articles. The court granted the government's motion. Ultimately, after appropriate labels had been designed, the articles were more than two years old and the articles were destroyed. (F.D.C. No. 62462; S. Nos. 79-204-269/71; N.J. No. 9)

FOOD ADDITIVES

Nature's Herbs comfrey, oatstraw, shavegrass (horsetail), & lobelia combination capsules; Nature's Herbs dandelion, golden seal, yellow dock root, & lobelia combination capsules; and **Nature's Herbs Desert Herb compound (desert tea), capsicum, & lobelia combination capsules,** at Miami, S. Dist. Fla.

Charged 3-6-81: when shipped by Nature's Herbs Inc., Orem, Utah, the articles contained the non-conforming food additive *Lobelia inflala L.*, since there was no regulation or exemption prescribing the condition for safe use of such food additive; 402(a)(2)(C). Default decree ordered destruction. (F.D.C. No. 63338; S. No. 81-239-904; N.J. No. 10)

Popsicle solutions in plastic tubes, at Searcy, E. Dist. Ark.

Charged 6-2-81: when shipped by Marshall Confections Inc., Marshall, Texas, the article, labeled in part "Freeze & Squeeze Popsie . . . assorted Pops. . . . Mfd. By C.D.P. Company . . . Oklahoma City, Okla.," contained the non-conforming food additive saccharin, since the product was not for a valid special dietary use and was not exempted; and saccharin had been substituted for sugar; 402(a)(2)(C), 402(b)(2).

Default decree ordered destruction. (F.D.C. No. 63477; S. No. 81-280-883; N.J. No. 11)

DRUGS/Human Use

Allopurinol tablets, at City of Commerce, C. Dist. Calif.
Charged 6-16-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (F.D.C. No. 63062; S. No. 80-245-421; N.J. No. 12)

Allopurinol tablets, and **other specified drug stocks,** at Malden, Dist. Mass.
Charged 3-12-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the District of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62867; S. No. 80-159-291 et al.; N.J. No. 13)

Barbiturate and analgesic combination tablets, at Greensboro, M. Dist. N.C.
Charged 2-17-81: when shipped by D.M. Graham Laboratories Inc., Hobart, N.Y., the article, labeled in part "Sedapap-10 Tablets . . . Mfg. by: Graham Labs., Hobart, N.Y. . . . Analgesic-Antitensive-Antipyretic . . . Mfg. for Mayrand Incorporated Pharmaceuticals, Greensboro, N.C.," was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (F.D.C. No. 63319; S. No. 81-162-996; N.J. No. 14)

Brompheniramine maleate & D-Isoephedrine Sulfate combination tablets, at Little Rock, E. Dist. Ark.
Charged 7-26-81: [when shipped by Pharmadyne Laboratories, Inc., Elmwood Park, N.J.], the article, labeled in part "Nadex sustained-Release Tablets . . . Brompheniramine maleate . . . D-Isoephedrine Sulfate . . . Distributed by Artex Laboratories, Inc.," had been manufactured, processed, packed and held under circumstances that failed to conform with current good manufacturing practice; 501(a)(2)(B). Default decree ordered destruction. (F.D.C. No. 63517; S. No. 81-280-887; N.J. No. 15)

Chlorthalidone tablets, at City of Commerce, C. Dist. Calif.
Charged 6-16-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (F.D.C. No. 63059; S. No. 80-245-421; N.J. No. 16)

Chlorpropamide tablets, at Lincolnwood, N. Dist. Ill.
Charged 4-4-80: when shipped by Darby Drug Co. Inc., Rockville Center, N.Y., the article, labeled in part "Rugby Chlorpropamide Tablets. . . . Manufactured for Rugby Laboratories, Inc., Rockville Center L.I., N.Y. . . . Manufactured by Chelsea Laboratories, Inc. Inwood, N.Y.," was a new drug without an effective approved New Drug Application; 505(a).

The manufacturer claimed the article, denied the charge, and asserted that the article was a generic version of "Diabinese," a brand of chlorpropamide tablets manufactued by another manufacturer who had marketed the Diabinese under an approved New Drug Application since prior to 1962. The claimant (manufacturer) of the article also claimed that even if chlorpropamide was once regarded as a new drug, generic chlorpropamide was not presently a new drug since it had been safely marketed for over 20 years, was safe, effective and generally recognized; that the claimant's article was manufactured according to rigorous quality standards; and that FDA's *Federal Register* statement that chlorpropamide was a "new drug" was not a binding administrative determination because FDA had not followed the requirements of the Administrative Procedures Act. The claimant cited the July 1979 district court finding in *Premo Pharmaceutical Laboratories Inc.* v. *U.S.A.*, U.S.D.C., S. Dist. N.Y., C.A. No. 78 Cir. 5435; and the claimant also asserted that, without waiving the claim that chlorpropamide was not a new drug, the claimant had filed with the FDA an Abbreviated New Drug Application, but FDA had not acted on such application.

The government served written interrogatories and requests for admissions of the claimant. Ultimately, a consent decree of condemnation ordered the article destroyed. (F.D.C. No. 62929; S. No. 80-111-998; N.J. No. 17)

Diethylpropion HCl tablets, at San Francisco, N. Dist. Calif.
Charged 3-8-78: when shipped by Pharmadyne Laboratories Inc., Hackensack, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). The article was claimed by the shipper. Pursuant to stipulation, the action was removed to the Eastern District of New York for consolidation for trial with a similar action. Ultimately, a consent decree ordered the article destroyed. (F.D.C. No. 62176; S. No. 79-179-687; N.J. No. 18)

Diethylpropion HCl tablets, trifluoperazine HCl tablets, doxylamine succinate with pyridoxine tablets, and **hydroxyzine HCl tablets,** at Bedford, Dist. Mass.
Charged 5-5-81: when shipped by Premo Pharmaceutical Laboratories Inc., South Hackensack, N.J., the articles were new drugs without effective approved New Drug Applications—505(a); and, while held for sale, the articles lacked adequate directions for use and were not exempted due to their new drug status—502(f)(1). Default decree ordered destruction. (F.D.C. No. 63461; S. No. 81-254-824 et al.; N.J. No. 19)

Furosemide tablets, at City of Industry, C. Dist. Calif.
Charged 7-14-81: when shipped by Superpharm Corp., Central Islip, N.Y., the article was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (F.D.C. No. 63500; S. No. 81-257-800; N.J. No. 20)

Furosemide tablets, two seizure actions, at Miami, S. Dist. Fla., and Hollywood, S. Dist. Fla.
Charged 10-21-81 and 10-21-81: when shipped by Superpharm Corp., Central Islip, N.Y., the article was a new drug without an effective approved New Drug Application; 505(a). Default decrees ordered destruction. (F.D.C. Nos. 62997, 63221; S. Nos. 80-193-506, 80-239-256; N.J. No. 21)

Furosemide tablets, chlorothiazide with reserpine tablets, and **trimethoprim with sulfamethoxazole tablets,** at St. Louis, E. Dist. Mo.
Charged 2-1-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action transferred to the Eastern District of New York for consolidation for trial with a similar action. Ultimately a consent decree ordered destruction. (F.D.C. No. 62823; S. No. 80-208-575; N.J. No. 22)

Furosemide tablets, and **diethylpropion HCl tablets,** at Tifton, M. Dist. Ga.
Charged 3-20-79 and amended 3-23-79: when shipped by Pharmadyne Laboratories Inc., Hackensack, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was removed to the Eastern District of New York for consolidation for trial with a similar action. Ultimately, a consent decree ordered destruction. (F.D.C. No. 62211; S. No. 79-100-578; N.J. No. 23)

Furosemide tablets, and **other specified drug stocks,** at Vienna, E. Dist. Va.
Charged 7-21-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). Default decree of condemnation ordered destruction. (F.D.C. No. 62781; S. No. 80-208-543; N.J. No. 24)

Hydroxyzine HCl tablets, allopurinol tablets, and **prochlorperazine capsules,** at Miami, S. Dist. Fla.

Charged 2-12-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62828; S. No. 80-166-696; N.J. No. 25)

Hydroxyzine HCl tablets, allopurinol tablets, trimethoprim with sulfamethoxazole tablets, and **metronidazole tablets,** at Brooklyn, E. Dist. N.Y.

Charged 6-23-80: when shipped by Pharmadyne Laboratories Inc., Hackensack, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). Pursuant to stipulation, the action was consolidated for trial with a similar action in the District of New Jersey. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 63009; S. No. 80-200-325; N.J. No. 26)

Hydroxyzine HCl tablets, diethylpropion HCl tablets, furosemide tablets, trimethoprim with sulfamethoxazole tablets, at Plainview, E. Dist. N.Y.

Charged 2-29-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the District of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree ordered destruction. (F.D.C. No. 62818; S. No. 80-208-578; N.J. No. 27)

Hydroxyzine pamoate capsules, at Tifton, M. Dist. Ga.

Charged 1-31-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). The article was claimed by the shipper. Pursuant to stipulation, the action was transferred to the District of New Jersey for consolidation for trial with a similar action. Ultimately, a consent decree of condemnation ordered the article destroyed. (F.D.C. No. 62779; S. No. 800-200-541; N.J. No. 28)

Hydroxyzine pamoate capsules, trimethoprim with sulfamethoxazole tablets, chlorthalidone tablets, hydroxyzine tablets, prochlorperazine tablets, and **spironolactone with hydrochlorothiazide tablets,** at Ferndale, E. Dist. Mich.

Charged 3-3-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the District of New Jersey for consolidation for trial with a similar action. Ultimately, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62767; S. No. 80-183-483; N.J. No. 29)

Iatric testosterone and estrone combination injectable, at Maryland Heights, E. Dist. Mo.

Charged 5-4-81: when shipped by Carter-Glogau Laboratories Inc., Glendale, Ariz., the article, labeled in part "Iatric I.M. Only . . . O'Neal, Jones & Feldman St. Louis, Missouri," was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (F.D.C. No. 63447; S. No. 81-236-068; N.J. No. 30)

Prochlorperazine capsules, at City of Commerce, C. Dist. Calif.

Charged 6-13-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (F.D.C. No. 63053; S. No. 80-245-421; N.J. No. 31)

Renacidin 10% sterile solution, at Rockford, N. Dist. Ill.

Charged 5-22-81: while held for sale after manufacture by K-N Enterprises Inc., Skokie, Ill., from interstate renacidin powder, the article was a new drug without an effective approved New Drug Application; and the labeling of the article lacked adequate directions for use and was not exempted due to the article's new drug status; 505(a), 502(f)(1). Default decree ordered destruction. (F.D.C. No. 63472; S. No. 81-248-686; N.J. No. 32)

Trimethoprim with sulfamethoxazole tablets, and **other specified drug stocks,** at Oklahoma City, W. Dist. Okla.

Charged 2-26-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the District of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62813; S. No. 80-208-572; N.J. No. 33)

DRUGS/Veterinary

Hexachloroethane suspension drench, at Sanford, M. Dist. Fla.

Charged 9-4-80: when shipped by Chemvet Laboratories Inc., Olathe, Kan., the article, labeled in part "Hexachloroethane Drench. . . . An Aid In The Elimination Of Mature Liver Flukes From Cattle, Sheep and Goats. . . . Manufactured for Veterinarian Specialties, Inc., Cedar Rapids, Iowa," was a new animal drug and no approval of a New Animal Drug Application was in effect with respect to its use or intended use; 501(a)(5).

Joe Baker of Baker Farms, Sanford, Fla., filed an answer on behalf of the article and denied the charge. However, no claim to the article was filed; the answer was not verified, and there was no statement of interest in the article or authorization for counsel to make a claim. Counsel for Baker Farms subsequently notified the government that Baker Farms did not intend to file a verified claim or to intervene in the action. Since no claim to the article was filed, the government moved for a default. A default decree of condemnation ordered the article destroyed. (F.D.C. No. 63139; S. No. 80-165-656; N.J. No. 34)

Neomycin sulfate & methyl violet solution spray, at Odin, S. Dist. Ill.

Charged 7-15-81: when shipped by Chem-Tech Ltd., Des Moines, Iowa, the article, labeled in part "Durvet Pink Eye Spray (Neomycin Sulfate, Methyl Violet). . . . Manufactured for Durvet Inc. Blue Springs, Missouri," was a new animal drug and no approval of a New Animal Drug Application was in effect with respect to its use or intended use; 501(a)(5). Default decree ordered destruction. (F.D.C. No. 63495; S. No. 81-261-921; N.J. No. 35)

Skin Medicine veterinary phenol and camphor combinations for horses and dogs, at Harrisburg, M. Dist. Pa.

Charged 8-14-80: when shipped by Jupiter Veterinary Products and its president, Jupiter, Fla., the article was a new animal drug and no approval of a New Animal Drug Application was in effect with respect to its intended use—501(a)(5); and the article had been manufactured, prepared, compounded and processed in an unregistered establishment—502(o). Default decree ordered destruction. (F.D.C. No. 63116; S. No. 80-228-127; N.J. No. 36)

MEDICAL DEVICES

X-ray system, Traceray IV, at Poulsbo, W. Dist. Wash.

Charged 10-16-79: the article, which had been manufactured by Western States Supply Ltd., Pueblo, Colo., was dangerous to health when used as directed, because the device would emit radiation beyond the pre-set exposure time—502(j); the accompanying labeling was false and misleading in claiming compliance with the regulation's standards, and in claiming that the device would deliver the radiation exposure stated in the instruction manual—502(a); and the article's quality fell below its purported quality—501(c). Consent decree authorized release to possessor for reconditioning. (F.D.C. No. 62559; S. No. 79-152-951; N.J. No. 37)

X-ray system, Traceray III, at Chaska, Dist. Minn.

Charged 10-2-79: the article, which had been manufactured by Western States Supply Ltd., Pueblo, Colo., was dangerous to health when used as directed, because the device would emit radiation beyond the pre-set exposure time—502(j); and the article's quality fell below its purported quality—501(c). Consent decrees ordered destruction. (F.D.C. No. 62612; S. No. 79-130-185; N.J. No. 38)

X-ray system, Traceray III, at St. Paul, Dist. Minn.
Charged 10-2-79: the article which had been manufactured by Western States Supply Ltd., Pueblo, Colo., was dangerous to health when used as directed, because the device would emit radiation beyond the pre-set exposure time—502(j); and the article's quality fell below its purported quality—501(c). Default decree ordered destruction. (F.D.C. No. 62617; S. No. 79-202-805; N.J. No. 39)

X-ray systems, Traceray III, 12 seizure actions, at Seaside, N. Dist. Calif.; Port Clinton, N. Dist. Ohio; Mountain View, N. Dist. Calif.; Squaw Valley, E. Dist. Calif.; Homestead, W. Dist. Pa.; Charleroi, W. Dist. Pa.; Moorhead, Dist. Minn.; Burnsville, Dist. Minn.; Grand Rapids, Dist. Minn.; North Branch, Dist. Minn.; Lebanon, M. Dist. Pa.; and Lemont, N. Dist. Ill.
Charged 10-5-79, 10-19-79, 10-5-79, 10-10-79, 10-12-79, 10-12-79, 10-10-79, 10-2-79, 10-15-79, 10-2-79, 10-16-79, 11-9-79: the articles, which had been manufactured by Western States Supply Ltd., Pueblo, Colo., were dangerous to health when used as directed, because the devices would emit radiation beyond the pre-set exposure time—502( ); the accompanying labeling was false and misleading in claiming compliance with the regulation's standards, and in that the devices would deliver the radiation exposure stated in the instruction manual—502(a); and the articles' quality fell below their purported quality—501(c). Consent decrees authorized release to the possessors' owners for reconditioning. (F.D.C. Nos. 62458, 62494, 62549, 62572, 62601, 62604, 62607, 62608, 62616, 62619, 62630, 62644; S. Nos. 79-150-776, 79-113-610, 79-150-339, 79-150-563, 79-204-545, 79-204-548, 79-129-256, 79-130-184, 79-218-506, 79-202-983, 79-204-615, 79-109-612; N.J. No. 40)

NOTICES OF JUDGMENT on Contempt Action

Spectro Foods Corp., and **Metamail Food Corp.** (Ernest O. Moenckmeir, president, Jeanene Moenckmeir, secretary-treasurer) at Summit, Dist. N.J.
Charged 1-24-76 in an order to show cause for contempt of temporary restraining order and preliminary injunction (see N.J. No. 44 of this issue of *FDA Consumer):* that the defendants had failed to comply with the recall order contained in the temporary restraining order and preliminary injunction.

After a hearing, the court found the two corporations in contempt and fined them each $5,000, plus $500 per day for each day of continued violation. The defendants appealed such adjudication as well as the issuance of the temporary restraining order and preliminary injunction upon which the contempt was based. Upon appeal, the court upheld the issuance of a preliminary injunction but vacated all of its provisions except Parts I and II (see N.J. No. 44 of this issue of *FDA Consumer).* However, the court ruled in favor of the defendants as far as the contempt action was concerned, saying:

The "Order for Civil Contempt"

"The 'Order for Civil Contempt' recites that it was issued when the defendant corporations disobeyed the recall order embodied in the TRO and the Preliminary Injunction. Since these recall provisions will be vacated, the court must now consider whether the 'Order for Civil Contempt' should continue in effect.

"While a defendant may be punished for criminal contempt for failing to obey an injunction which is later set aside, the same result does not follow in a civil contempt proceeding. The difference in treatment follows from the fact that whereas a criminal contempt order is punitive—to vindicate the authority of the court, the purpose of a civil contempt order is remedial—to coerce compliance with the injunction or recompense a party for losses caused by non-compliance. The right to remedial relief disappears when it is determined that an injunction was issued erroneously. Therefore, to the extent the contempt order is correctly described as a 'civil contempt,' it falls with the vacation of the recall order on which it was based.

"Although the district court characterized its order as one for civil contempt, appellate courts must look to the substance of the order rather than the form to determine whether the contempt is civil or criminal in light of the nature and purpose of the sanction. The fact that a defendant can purge himself of the contempt and avoid the sanctions indicates that the purpose is coercive and the contempt order is civil. Sanctions which are imposed unconditionally strongly suggest a punitive purpose and a criminal contempt. However, an unconditional fine paid to the opposing party is a compensatory civil contempt.

"In its 'Order for Civil Contempt,' the district court adjudged the two corporations in contempt and fined them each $5000 plus $500 for each day they continue to violate the recall provisions of the TRO and the Preliminary Injunction. The continuing $500 per day fine is unquestionably for civil contempt: It is clearly coercive since it can be avoided by compliance. The flat $5000 fine, however, seems more in the nature of punishment for past violations of the court's orders, and there is abundant evidence that the court's purpose in imposing it was punitive rather than coercive or remedial. Nevertheless, in light of the considerations discussed below, we vacate the 'Order for Civil Contempt' in its entirety.

"First, it is possible that there was a remedial purpose underlying the $5000 fine. The fine is payable to plaintiffs, the government, and could be viewed as compensation for their efforts in monitoring defendants' (non)compliance with the TRO and the Preliminary Injunction. Alternatively, the flat fine might have been coercive, to emphasize that the court fully intended to impose the daily fine in the event of further noncompliance, thus increasing the *in terrorem* effect of the daily fine.

"Second, even if the fine were for criminal contempt, it could have been imposed only in a criminal contempt proceeding conducted in accordance with the Criminal Code, 18 U.S.C. §§401, 402 and Rule 42 of the Federal Rules of Criminal Procedure, as well as the constitutional provisions relevant to criminal trials. In the instant matter due process was not satisfied in the form of notice to defendants of a pending criminal contempt charge including describing it as such as required by F.R.Cr.P. 42(b).

"In the matter of criminal contempt, as in all criminal cases, due process also requires that a defendant is presumed innocent and punishment can only be imposed after the government has met its burden of establishing defendants' guilt beyond a reasonable doubt. Yet on several occasions the district judge indicated that defendants' guilt had been established when the first Order to Show Cause was issued and that defendants thereafter had the burden of proving their innocence of the contempt charges. Insofar as defendants were convicted of criminal contempt, adherence to procedural due process requires reversal of the conviction." (Inj. No. 710; S. No. 76-35-128 et al.; N.J. No. 41)

NOTICES OF JUDGMENT on Injunction Actions

Bel-Mar Laboratories Inc., Hannah Schechter, president, and **Stephen B. Schechter,** secretary-treasurer, Inwood, E. Dist. N.Y.
Charged 12-16-76 in a complaint for injunction: that the defendants, at their Inwood, N.Y., plant, manufactured, processed, packed, labeled, held for sale after shipment of interstate components and distributed in interstate commerce certain drugs (i.e., sterile injectable drugs in the form of solutions, aqueous suspensions and oil preparations; that the circumstances used for the manufacture, processing, packing and holding of the drugs failed to conform with current good manufacturing practices; that FDA inspections disclosed a number of specified deviations from current good manufacturing practices; that, indicative of the

defendants' failure to adequately sterilize drugs, FDA examination found *Corynebacterium equi* (a bacteria found in pregnant mares' urine, the source of estrone) in samples of the defendants' estrone aqueous suspension; that a number of the defendants' drugs were violative as follows: the drugs were U.S.P. or N.F. drugs and their strength differed from and their quality fell below their purported strength or quality; the drugs' labeling contained false and misleading statements with respect to the sterility and quantity of the articles; and the drugs were dangerous to health when used as directed in their labeling; and that the defendants are well aware that their activities are in violation of the law; 501(a)(2)(B), 501(b), 501(c), 502(a) and 502(j).

The action came on for a hearing before the court. The court ruled in favor of the government and authorized a permanent injunction. The defendants litigated the proposed terms of the decree and asserted that an arbitrator should be appointed. Subsequently, the court issued an order of permanent injunction which enjoined the complained of acts and specified which articles on hand could be shipped. (Inj. No. 755; S. No. 76-40-927 et al.; N.J. No. 42)

Barfred Research Laboratories Inc., and **Benjamin Z. Friedman,** president, Coral Gables, S. Dist. Fla.

Charged 6-2-78 in a complaint for injunction: that the defendants had been, at their Coral Gables, Fla., plant, manufacturing, processing, packing, labeling, holding and distributing various drugs which had had components shipped in interstate commerce; that the circumstances used for the drugs' manufacture, processing, packing and holding failed to conform with current good manufacturing practices; that the strength of a number of the drugs differed from purported strength; that the labels of a number of the drugs failed to bear the name and place of business of the manufacturer; that the labels of a number of the drugs failed to bear an accurate statement of the quantity of contents; that the labels of a number of the drugs lacked the established name of each active ingredient; that the labels of a number of the drugs, which were packaged in bulk form for further processing, packing or manufacturing lacked adequate directions for use and were not exempted, since the labels lacked the required statement "Caution: For manufacturing, processing, or repacking"; that FDA inspections had revealed a number of specified significant deviations from current good manufacturing practices; and that, because of specified written and oral notice and a number of specified recalls, the defendants were well aware that their activities were in violation of the law; 501(a)(2)(B), 501(c), 502(b)(1), 502(b)(2), 502(e)(1)(A)(ii) and 502(f)(1).

A consent decree enjoined the complained of violations, enjoined the distribution of all drug components on hand, and ordered recalls of all drugs shown to be adulterated or misbranded. (Inj. No. 855; S. No. 78-141-013 et al.; N.J. No. 43)

Spectro Foods Corp., Metamail Food Corp., and **Ernest O. Moenckmeier,** president, and **Jeanine Moenckmeier,** secretary-treasurer, Summit, Dist. N.J.

Charged 1-19-76 in complaint for injunction: that the defendants caused the manufacturing, processing, packing, labeling and holding for sale (after interstate shipment of components) "Bitter Food Tablets" containing amygdalin in strengths of 100 mg and 500 mg per tablet; that the defendants wholesaled the tablets using a Spectro Food Corp. label and retailed the tablets using a Metamail label; that when distributed in interstate commerce, and while held for sale, the article "Bitter Food Tablets" was a non-conforming food additive, was a drug lacking adequate directions for use, since the intended purpose and condition of use (i.e., the treatment and prevention of cancer) were not stated, was a drug lacking adequate warnings against unsafe use, and was lacking the prescription legend; that, as an integral element of their promotion of amygdalin tablets, the defendants employed a pamphlet, reading in part "The Nieper Approach ('Nieper Regimen') to Biological Cancer Treatment . . . based upon: * * * 4) the treatment with nitrilosides (non-toxic
carcinostatic substances)"; that the article "Bitter Food
new drug without an effective approved New Drug A
Mr. Moenckmeier had admitted to previous distributic
tablets; that the individual defendants had refused to dis
of amygdalin, the active ingredient in "Bitter Food Ta
stocks of the tablets were stored; 402(a)(2)(C), 502(
503(b)(4), 505(a).

The court entered a Temporary Restraining Order
the manufacture and distribution of Bitter Food Tal
further ordered Spectro Foods Corp. to recall all previc
tablets within the next five days. After an *ex parte* he
issued an order to show cause why the defendants shou
contempt for failure to comply with the recall order. Sh
after a hearing on the alleged contempt and on
preliminary injunction, the court issued a preliminary i
a compliance schedule and held the contempt matters i
government moved for a second order to show cause
order should not issue (See N.J. No. 41 of this
Consumer.) The defendants appealed the temporary re
the preliminary injunction and the contempt order.

Upon appeal, the court of appeals found that the pa
porary Restraining Order and Preliminary Injunctio
FDA supervisory power over the conduct of the defe
were unwarranted; and except for parts I and II of the
junction, the court vacated the injunction and remande
further proceedings. The court said:

"Presently before the court is an appeal from a Prel
tion secured by the government pursuant to the Fede
and Cosmetic Act ('the Act'), 28 U.S.C. §332(a), and fr
Civil Contempt arising out of alleged violations o
Restraining Order and the Preliminary Injunction. Th
Spectro Foods Corporation ('Spectro') and Metamail
tion ('Metamail'), both New Jersey corporatio
Moenckmeier, president, and Jeanine Moenckm
treasurer of the two corporations. They manufacture
product known as 'Bitter Food Tablets' which they alle
use in the treatment of cancer. The complaint alleged
Tablets contain amygdalin which is an 'unsafe' 'food a
tablets themselves are a 'food,' a 'drug' and a 'new d
quently that the defendants were in violation of sectio
(k) by virtue of their manufacture, distribution and ho
an 'adulterated food,' a 'misbranded drug' and an u
drug.'

"At the time the complaint was filed on January 19,
judge entered a Temporary Restraining Order
restrained the manufacture and distribution of Bitter F
the government's urging that the public safety was je
current availability of these tablets, the court further or
recall all previously distributed tablets by Januar
procedural development was an *ex parte* hearing he
January 24. The result of the January 24 hearing was t
order to show cause why defendants should not be held
failure to comply with the recall order.

"A hearing was held on January 28 to deter
preliminary injunction should issue and whether defe
held in contempt for violation of the TRO. At that tim
schedule was set up and the contempt matter held in ab
trict judge also made findings of fact and conclusion
January 29, he issued a preliminary injunction, the s
contested in this appeal. The Preliminary Injunction
porated the restraints on manufacture and distributio
order of the TRO, but also restrained the distribution
ditive or drug in violation of the Federal Food, Dru

Act. The court added further provisions which, in effect, ordered the FDA to supervise and control the conduct of defendants' business.

"On February 9, the government, having concluded that the defendants had defaulted on the agreed upon compliance schedule, moved for a second order to show cause why a contempt order should not issue. At a hearing on February 17, the corporate defendants, Spectro and Metamail, were found in contempt for noncompliance with the recall order contained in the TRO and the Preliminary Injunction, and on the following day the district judge issued an 'Order for Civil Contempt.'

"The defendants responded on February 20 by filing notice of this appeal from the TRO, the Preliminary Injunction and the Order for Civil Contempt. On February 27, a judge of this court denied a stay of these three orders.

I. Jurisdiction of the Reviewing Court

"The Preliminary Injunction is a reviewable interlocutory order under the jurisdiction conferred by 28 U.S.C. §1292(a)(1). Although an order of civil contempt is not ordinarily appealable, one who is a party may appeal from a civil contempt order in connection with some other appealable order, including a preliminary injunction. Consequently, the court has jurisdiction over the appeal from the Order for Civil Contempt.

"A TRO is not an injunction and consequently is not an appealable order. Further, any purported notice of appeal from the TRO was not timely filed and the TRO had, by its terms, expired prior to the appeal. The court therefore need not consider whether the provisions of the TRO which did more than merely temporarily restrain defendants converted it into a form of an interlocutory injunction independently reviewable under 28 U.S.C. §1292(a)(1). The contempt order, however, does purport to be based in part on defendants' non-compliance with the TRO. Although this court has no jurisdiction to entertain an appeal from the TRO, the validity of the TRO must nonetheless be examined for the limited purpose of our review of the Order for Civil Contempt which the district court issued because of the defendants' failure to comply with the recall provisions of the TRO and Preliminary Injunction.

II. Validity and Scope of the Preliminary Injunction

"Defendants have alleged a plethora of procedural defects in the district court proceedings. Most of these are wholly without merit, and the remainder, though in some respects disturbing, do not warrant reversal of the entire order granting the Preliminary Injunction. However, because several provisions of the Preliminary Injunction are far broader than the record justifies and others exceed the permissible scope of interlocutory relief, some portions of the Preliminary Injunction are invalid.

"The prohibition of the manufacture and distribution of the Bitter Food Tablets or other amygdalin-containing articles in parts I and II of the Preliminary Injunction (and parts I and II of the TRO) are unobjectionable. The FDA affidavits indicated that amygdalin is a food additive not on the list of additives generally recognized as safe ('GRAS') and is a new drug for which no New Drug Application is on file. Other affidavits concerning defendants' manufacture and distribution of the Bitter Food Tablets provided a sufficient basis for the district court's preliminary conclusions that defendants violated 21 U.S.C. §331(a), (d) and (k) by virtue of their manufacture, distribution and holding for sale of Bitter Food Tablets. Parts I and II of the TRO and the Preliminary Injunction are properly tailored to enjoin these particular violations of the act.

"The restraints in parts III and IV of the Preliminary Injunction are far broader than those in parts I and II. While parts I and II are limited to restraints on the manufacture and distribution of Bitter Food Tablets and other amygdalin-containing articles, parts III and IV prohibit the distribution of *any* article of food containing a food additive not recognized as safe or any new drug for which no new drug approval application has been filed. This broad injunctive restraint was issued notwithstanding that the court had no evidence concerning distribution by defendants of any unsafe food additive or unapproved new drug other than the Bitter Food Tablets.

"The district courts are invested with discretion to model their orders to fit the exigencies of the particular case, and have the power to enjoin related unlawful acts which may fairly be anticipated from the defendants' conduct in the past, but a decree cannot enjoin conduct about which there has been no complaint. All the alleged violations here stemmed from the manufacture and distribution of a single item. There was no evidence of record from which the district court could fairly have anticipated that defendants would distribute other substances in violation of the act, nor did the court make any such findings. The use of the broad injunctive language on so scant a record constitutes error. Parts III and IV of the Preliminary Injunction will be vacated.

"The primary controversy and that which led to issuance of the contempt order centers upon part V of the Preliminary Injunction and part III of the TRO. Those provisions employ identical language and encompass the recall order directing defendants to: (a) notify an FDA representative of the location and amount of all stocks of Bitter Food Tablets, amygdalin and associated labeling; (b) notify all recipients of the Bitter Food Tablets to return them to defendants; (c) provide an FDA representative with a copy of said notice and a list of all persons to whom the Bitter Food Tablets had been distributed; (d) obtain statements from each recipient of the Bitter Food Tablets as to amount of the article received, the amount returned, and disposition of that which was not returned; and (e) make copies of the customer statements available to an FDA representative.

"Those aspects of the recall order which culminated in the Order for Civil Contempt did not merely operate to restrain further violations of the act by defendants for, according to the record, they involved items no longer in defendants' possession. Neither did the recall order operate *pendente lite* to preserve the status quo, i.e., 'the last actual uncontested status which preceded the pending controversy.' Rather, the recall provision functioned as though it were 'actually a discovery provision,' as the district court characterized it, enabling the government to locate various quantities of the tablets for seizure pursuant to 21 U.S.C. §334.

"The power to issue a preliminary injunction, especially a mandatory one, should be sparingly exercised. Parts I and II of the Preliminary Injunction are based on the alleged violation of 21 U.S.C. §331(a)(d)(k), and therefore do not require a showing of immediate and irreparable injury. On the other hand, the recall order does not address a particular violation of the act from which injury may be presumed and thus there must be an independent showing of irreparable harm to warrant its issuance.

"The district court made no finding that the public would be irreparably harmed absent a recall order. In fact, the court made no specific findings of irreparable injury other than that resulting from defendants' violation of the act itself. In this circumstance it was error for the court to issue an interlocutory mandatory injunction unsupported by specific findings of irreparable injury *Cf. A. O. Smith Corp. v. FTC*, 530 F.2d 515, 525 (3d Cir. 1976).

"From this discussion of part V of the Preliminary Injunction and part III of the TRO, it is equally apparent that the order granting the FDA supervisory power over the conduct of defendants' business was wholly unwarranted. The order forbids defendants from distributing or holding for sale any article of food or drug without the FDA approval, requires the FDA to sequester defendants' inventory and their entire stock of raw materials and to destroy all items which it does not 'approve.' Further, the decree orders defendants to abide by the decisions of the FDA representative, to compensate the government for the cost of this supervision, and generally enjoins defendants from selling or disposing of any article of food or drug in violation of the act or the laws of any state or territory.

"This far-reaching order *might* appropriately be included in a permanent injunction issued after a full evidentiary hearing disclosed a history of repetitive, flagrant violations, suggesting a real danger of recurrent evasions of a more carefully drawn order. However, in the context of this interlocutory order, based on a narrow showing by affidavit, the government's request for such a broad order can only be characterized as gross over-reaching. In the absence of any relevant findings of irreparable injury, the court's acquiescence evidenced by the grant of the order constitutes both an abuse of its discretion and 'a serious mistake in considering the proof.' *Cf. A.O. Smith Corp.* v. *F.T.C., supra,* at 525."

Subsequently, a hearing was held on a permanent injunction. The defendants indicated their desire to enter into a consent decree. A consent decree permanently enjoining the complained of violations was filed. (Inj. No. 710; S. No. 44-986H et al.; N.J. No. 44)

NOTICES OF JUDGMENT on Miscellaneous Actions

Menstrual tampon Rely, its classification by FDA as a device, and **alleged hazards and injuries,** San Francisco, N. Dist. Calif.

Charged 9-23-80 by Carol A. Thompson and Barbara Lee, against Procter & Gamble Co., H.H.S. Secretary Patricia Roberts Harris, FDA Commissioner Jere Goyan, and Bureau of Medical Devices Director Victor M. Zafra, in a class action complaint for judicial review, mandamus, injunction and other relief (e.g., restitution and damages): that Procter & Gamble Co., Cincinnati, Ohio, had manufactured and marketed Rely tampons; that Rely tampons were promoted as a revolutionary new kind of tampon consisting of tiny sponges and super absorbent synthetic fibers; that Rely tampons achieved their primary purpose through chemical action; that FDA had failed to classify the tampons as a new drug, had improperly classified the tampons as a medical device, and had improperly delegated authority over the tampons to the Bureau of Medical Devices who had improperly classified the tampons, first as class I devices and subsequently as class II devices; that, even after reports indicated that the tampons posed a serious threat to all women using them, FDA had failed to require affirmative proof of safety and effectiveness, and had allowed continued marketing; that FDA had a plain, clear and non-discretionary duty to classify the tampons as a class III device; that, in February, March, April and May of 1980, plaintiff Thompson had experienced adverse symptoms while using the tampons and had to be taken to the hospital in June of 1980; that plaintiff Lee had experienced adverse symptoms while using the tampons for approximately one year and in March 1980 had been hospitalized for eight days and confined to an intensive care unit for approximately three days; that the defendant Procter & Gamble Co. had been unjustly enriched; that the plaintiffs sought restitution, compensatory and punitive damages, judicial review and declaratory judgment, injunctive relief, mandamus, and award of attorneys' and experts' fees and costs of the suit.

The plaintiffs served written interrogatories and a request for the production of documents in the possession of the government. The government moved to dismiss, asserting that FDA had already negotiated a consent agreement with Procter & Gamble Co. under which: (1) Rely had been withdrawn from the market; (2) Rely may not be reintroduced without FDA's prior written permission; (3) a warning to cease using Rely was extensively advertised; and (4) unused Rely was retrieved and the purchase price was refunded; that, because Rely was no longer on the market, the plaintiffs' claims against the government were moot; that the action should also be dismissed because: (1) The classification of medical devices and drugs was within FI
and thus not subject to mandamus; (2) there was no jur
the Administrative Procedures Act; and (3) the plaintifl
exhaust their administrative remedies.

The court dismissed the actions against the federal o

"This case concerns Procter and Gamble's Rely b
which plaintiffs allege are unsafe. In addition to Procte
plaintiffs have sued several federal officials. The federa
moved to dismiss the action as against them for failure
on which relief can be granted.

"The two counts against the federal defendants sec
nature of mandamus directing the Food and Drug Ad
reclassify Rely tampons. However, the existence of alte
precludes such an action. *Kennecott Copper Corp.,*
Division v. *Costle,* 572 F.2d 1349, 1356 (9th Cir. 1978).
have not alleged that they have exhausted their administ
or that it would be futile to do so. They may be able to
they seek by petitioning the Food and Drug Administrat
21 U.S.C. §360c(e) or 21 C.F.R. §10.25. Accordingly,
dered that counts XV and XVI of the complaint are

"It is hereby further ordered that the federal defend
dismiss is granted and that the action is dismissed aga
Patricia Roberts Harris, Secretary of the Departmen
Human Services, Jere Goyan, Commissioner of the Fo
ministration, and Victor M. Zafra, Director of the Bur
Devices." (Misc. No. 616; N.J. No 45)

NOTICE OF JUDGMENT on Criminal Actio

Francois Savery, clinical investigator, Long Beach, C. Dist.

Charged 7-9-81 by grand jury: that, in a matter within
tion, the defendant, knowingly and willfully, submitted
and document containing false and fraudulent material s
an SMA 12/60 chart dated June 17, 1976, representin
blood tests; 18 U.S.C. 1001. Guilty plea; $5,000 fine
probation with special conditions, including not pract
unless lawfully licensed and taking no part in the c
medical research investigation in connection with the
plications. (F.D.C. No. 61861; S. No. 78-25-604 et al.

Notices of Judgment are given pursuant to section 705
Food, Drug, and Cosmetic Act. Notices of Judgment report
seizure proceedings, criminal proceedings, and injunctio
Seizure proceedings are civil actions taken against *goods* a
violation, and criminal and injunction proceedings are a
individuals charged to be responsible for violations. The
involve foods, drugs, devices, or cosmetics which were alle
terated or misbranded or otherwise violative of the law w
into and while in interstate commerce, or while held for sale
in interstate commerce.

Notices of Judgment are prepared by Food and Drug
of the General Counsel, HHS.

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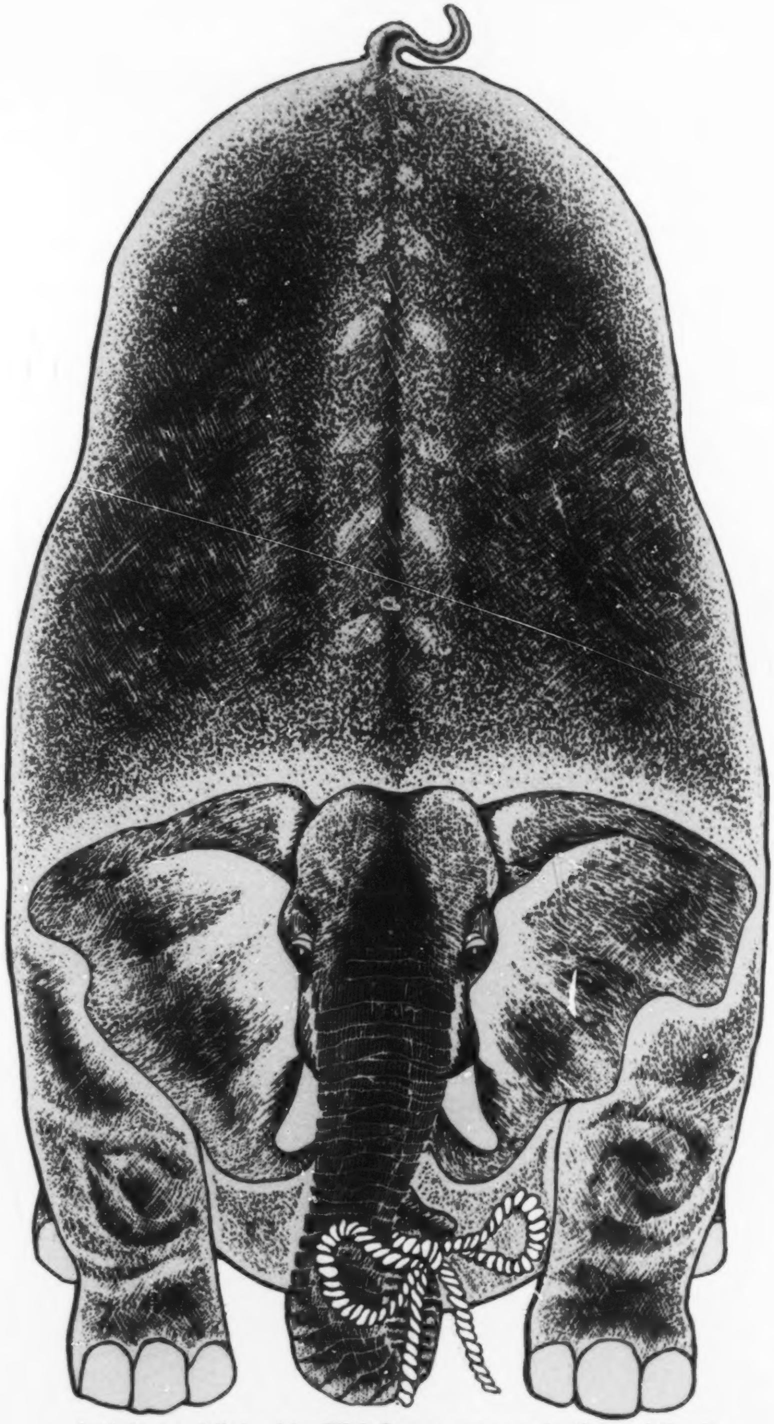

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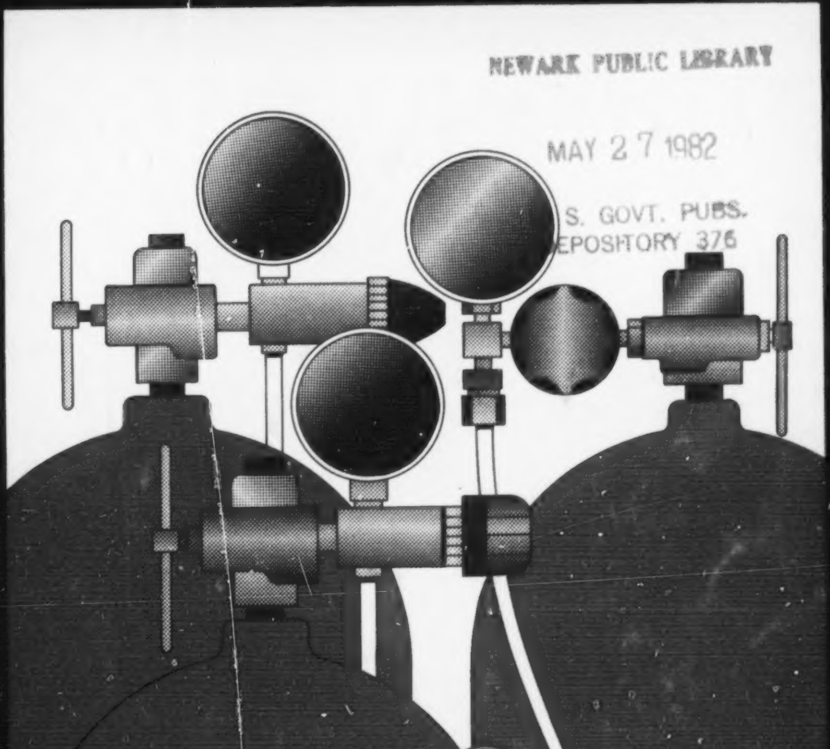

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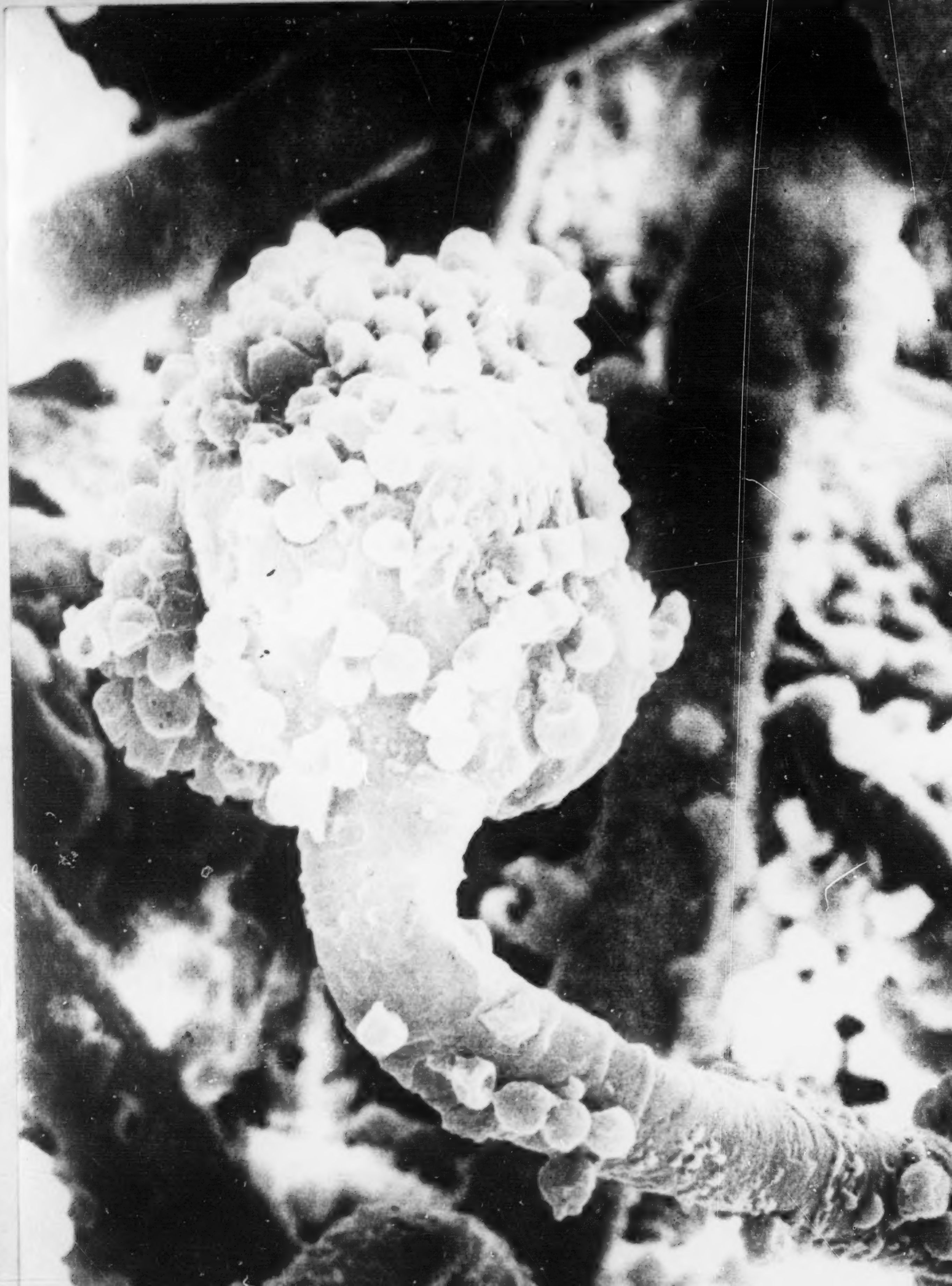

FDA CONSUMER

VOL. 16 NO. 4 **MAY 1982**

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The food we eat takes an adventurous route through our digestive systems. The process starts in the mouth when saliva goes to work. It ends some 30 feet and 24 hours later.

When Carp Was Dressed Up Like Tuna 10
Carp is carp (and some say not edible) and tuna is tuna. A Minnesota entrepreneur once tried to pass off carp as tuna. (It didn't work.)

Gases Are Drugs, Too 12
Ordinary air and manufactured air are among the 10 gases used for medical purposes in this country. The gases are considered drugs for regulatory purposes.

Rodents Shed Evidence 16
The science of trichology is the study of hairs, and rodents often leave behind much study material as they make their ways through areas in which foodstuffs are stored.

On Narrowing the Patient-Doctor Communications Gap 19
The American Medical Association and a major pharmaceutical firm are among the groups that have come up with patient education programs which could replace the now-shelved patient package insert (PPI) idea proposed by FDA.

About the Fungus Among Us 22
Fungal disease sources are not limited to ancient tombs but lie in wait in many forms in the United States and other countries. Some of the fungi involved occur even in common soil.

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Not an escapee from a science fiction movie, this fascinating creature is a fungus by the name of* Aspergillus fumigatus, *photographed under an electron microscope by John Ewell of FDA's Bureau of Biologics.* A. fumigatus *is the cause of aspergillosis, one of the most common human fungal infections in this country. There's more about fungi and the devastation they bring in* About the Fungus Among Us *on page 22.

Richard S. Schweiker
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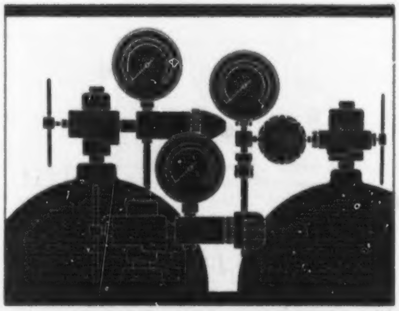

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Updates

ALOE
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BEAUTY
LOTION
4 OZ.

More on Aloe Vera

In the November 1981 issue of *FDA Consumer*, we published a letter from J. Robert Brouse, National Aloe Science Council Inc., who took exception to our article on Aloe Vera ("The Overselling of Aloe Vera," July-August 1981). Another reader has responded to Mr. Brouse's comments:

Pages 29 and 30 of the November '81 issue of the FDA Consumer *spurred me to write this letter. As a registered clinical dietitian, I wish to say hooray for your article on Aloe Vera in the July/August '81 issue of the* FDA Consumer. *I see too many vulnerable consumers buying this "wonder drug" for curing literally anything, at an outrageous cost.*

J. Robert Brouse . . . is misinformed in the area of nutrition. It is highly unlikely that Aloe Vera, a plant, contains "all essential amino acids"; we find all of the essential amino acids in foods with animal origin. If it is "complex sugars" we wish to increase in our diet, we need only turn to potatoes, corn, breads and cereals. . . . Unfortunately, only one or two vitamins naturally predominate in a single plant source, which is one reason why we are encouraged to eat a variety of foods—to be sure to touch on the various vitamins and minerals distributed through a wide range of foods. . . .

Melinda Hemmelgarn, B.S., R.D.
Clinical Dietitian
Columbia, Mo.

Emphasis on Orphan Drugs

Health and Human Services Secretary Richard S. Schweiker has announced his intention to establish an orphan drugs and products board to coordinate and speed the research, development and approval of designated orphan drugs.

The term "orphan" is applied to drugs and products that are useful in the diagnosis or treatment of rare diseases but for which only a small market exists. The problems faced by those who need these drugs and the reasons why they don't get on the market were reviewed in "Rx For Orphan Drugs" in the September 1980 *FDA Consumer.*

"There is a great deal of justified interest in orphan drugs by the Congress, the drug industry and the public," Secretary Schweiker said in his announcement. "Our objective is to encourage the prompt development and availability of proven orphan drugs to save lives and treat these diseases, while safeguarding patient health and safety."

The board will submit a progress report to the Congress within a year of its formation, Schweiker said.

The board will be chaired by the assistant secretary for health, Dr. Edward N. Brandt Jr., and will draw its membership from the Food and Drug Administration, the National Institutes of Health, the Centers for Disease Control, the Alcohol, Drug Abuse and Mental Health Administration and the Health Care Financing Administration.

Other relevant departments and agencies, such as the Department of Defense, the Veterans Administration and the Department of Commerce, will name representatives to the board.

Pump Delivers Cancer Drug

An implantable infusion pump, one of the new drug delivery systems described in "New Routes for Drugs to Travel" *(FDA Consumer*, March 1982), has been approved by FDA for delivering an anti-cancer drug, fluorouridine, directly to a cancer-ridden liver, and for dispensing heparin to prevent blood clots and treat disorders such as phlebitis.

The pump, about the size of a hockey puck, contains a compressed liquid which slowly expands and pushes the active drug through a plastic tube into a blood vessel. A physician can refill the pump with a hypodermic needle, which penetrates the patient's skin and a rubber membrane on the device.

Previous drug pumps were worn outside the body and delivered their drugs via catheters that pierced the skin.

When used in treating liver cancer, the pump delivers fluorouridine directly to the site of the tumor. Very little of the drug reaches the rest of the body. This helps to avoid many of the side effects often associated with cancer therapy, such as nausea, vomiting and lowered blood cell count.

Studies at the University of Michigan also found the pump capable of delivering drug levels to the tumor up to 400 times greater than those possible through methods such as intravenous infusion in a hospital.

In studies using the pump to treat blood disorders, 92 percent of the patients with previously untreatable clotting problems were completely free of recurring disease during the period of the study. Not only did the pump deliver effective treatment, it also spared patients the expensive, troublesome and often painful regimen of multiple daily heparin injections or long-term hospital confinement.

Invented by Dr. Henry Buchwald of the University of Minnesota, the pump is manufactured by the Infusaid Corp. of Sharon, Mass. It is made of stainless steel, titanium and silicon rubber, weighs about 6.3 ounces and is 3.5 inches across and about an inch thick. The pump is refilled once a week to once a month, depending on the patient's needs.

In experimental use in 137 patients for as long as 40 months, there were five pump failures, none of which caused serious complications. The device is also being studied for dispensing drugs to treat brain tumors and insulin for diabetes.

Another Cancer 'Cure'

Despite the lack of scientific evidence that they work, unproven cancer cures still abound. The latest to hit the headlines is "immuno-augmentative therapy." In March, Oklahoma Gov. George Nigh signed legislation approved unanimously by both chambers of the state legislature to permit the prescribing and administration of the therapy in the treatment of any malignancy, disease, illness or physical condition. Last year the governor of Florida vetoed similar legislation.

Actually, the immuno-augmentative therapy is not new. In December 1974, Rabbi Widom, president of the Immunology Research Foundation, Great Neck, N.Y., submitted to FDA's Bureau of Biologics an investigational New Drug Application seeking to initiate human investigational trials with "immuno-augmentative therapy." Lawrence Burton, an experimental zoologist with a 1955 doctoral degree from New York University, was to be the principal investigator.

Bureau questions about the research were not fully answered despite several exchanges of correspondence. Clinical studies were never approved, and in March 1976 the application was placed in the bureau's inactive files with the understanding from Rabbi Widom that any human trials would be confined to the state of New York. The foundation has never attempted to reactivate the file.

However, according to news media accounts, in 1976 Burton opened the Immunology Researching Centre in Freeport on Grand Bahama Island, where he has been treating cancer patients with injections of a "secret blood serum" alleged to increase the body's immunity against the formation of cancer cells. Fees reportedly range up to $7,500 per patient, excluding transportation and local housing costs.

In January of 1978, at the request of the Bahamian government, a physician representative of the National Cancer Institute visited the Freeport clinic. He asked for a sample of the serum for independent testing, but was refused. Accordingly, it is NCI's position that there is no basis for evaluation of "immuno-augmentative therapy" and no evidence that it is effective against cancer.

The American Cancer Society's Unproven Methods of Cancer Management Committee, the American Medical Association and NCI are aware of Dr. Burton's practice. They and FDA counsel patients to avoid this unproven treatment and to remain in the care of qualified physicians.

Diet Aid Controversy

FDA says for the moment it disagrees with an expert panel's recommendations on the proper dosage for phenylpropanolamine, an ingredient in popular over-the-counter diet aids.

In a preamble to the panel report, published for public comment in the Feb. 26 *Federal Register*, FDA noted that reports published in the medical literature after the panel report was submitted indicate that phenylpropanolamine doses higher than those currently marketed (but within the range recommended as safe by the panel) cause elevation of blood pressure. Other studies, reviewed by the panel, showed no such effect at currently marketed dosages. FDA called for more research to determine a safe dose range for phenylpropanolamine and the extent to which the ingredient induces or aggravates high blood pressure.

Until this is accomplished, FDA will permit phenylpropanolamine to be used at current levels for which there is a history of use in weight control but will not permit the higher dose diet aids as recommended by the panel and available abroad. Traditional U.S. levels total 75 milligrams or less per day. The panel had said doses of up to 150 milligrams would be safe.

The panel, which reviewed 113 ingredients sold in non-prescription diet aids, said only two, phenylpropanolamine and benzocaine, are safe and effective for weight control. The review was part of FDA's evaluation of all ingredients sold in non-prescription, or over-the-counter (OTC), drugs. What the panel had to say about the other 111 ingredients and the labeling claims made for OTC diet products was the subject of the article "Experts Weigh Reducing Potions" in the October 1979 *FDA Consumer*.

Happenings Along The GI Tract

by Annabel Hecht

The juice, eggs, toast and coffee that a person eats for breakfast take about 24 hours to be digested and absorbed. During this time, the food and drink travel through about 30 feet of internal channels. The substances are churned and mixed with some powerful acids secreted along with enzymes. The route traveled is known as the alimentary canal, or the gastrointestinal (GI) tract, and goes from the mouth to the anus, the last segment of the rectum.

Digestion begins in the mouth where food is broken up by chewing and then mixed with saliva containing the enzyme amylase, which begins the breakdown of starch to sugar. Swallowing carries the food into the esophagus and sends it on its way to the stomach. Time down the 10-inch long esophagus varies by no more than a few seconds, depending on whether what is swallowed is a liquid or a solid.

The stomach is not located just below the belt line, as many people think, but is much higher up, on the left side of the abdomen just under the diaphragm. The stomach serves as a kind of holding tank where the food is further churned and mashed by its rhythmic contractions. Starch digestion continues and pepsin breaks protein down into simpler compounds. Pepsin needs the help of hydrochloric acid. The two substances are released from stomach cells by gastrin, a hormone that is stimulated by the presence of food in the stomach.

After it is thoroughly mashed and mixed, the food, now called chyme, moves into the small intestine through the pylorus, a muscular valve at the lower end of the stomach. Because the small intestine can handle only so much, the pylorus allows only a small amount of chyme through at a time. Carbohydrates, which require less work from the digestive system, move through the pylorus faster than high protein and fat foods. This may explain why Chinese meals, which tend to be more vegetable than meat, seem to leave the diner feeling hungry soon after the meal is over.

The small intestine, named for the size of its diameter rather than for its 20-22 foot length, consists of three sections: the duodenum, the jejunum and the ileum. In the duodenum chyme is subjected to pancreatic juices and bile from the liver. These juices neutralize the hydrochloric acid and cause a further breakdown of carbohydrates, proteins and fats. The final digestion of chyme and the absorption of nutrients takes place in the jejunum and ileum. Absorption takes place through the actions of tiny hair-like projections, called villi, that line the intestines. Fats and fat soluble components are carried partly to the liver and partly to the blood via the lymphatic system. Vitamins, minerals, amino acids and sugars travel to the liver, the body's key unit in the processing of nutrients. By the time the chyme has completed its passage through the small intestine, 95 percent of the nutrients have been absorbed. What's left is sent on to the large intestine, or colon, which takes care of the absorption of water and electrolytes—i.e., sodium, potassium, chloride and bicarbonate. What can't be absorbed is concentrated as fecal matter and periodically eliminated.

So much for breakfast.

Except for the conscious act of chewing and swallowing, most people don't give much thought to the digestive process. It is completely automatic. But ever so often they become acutely aware of the existence of the gastrointestinal tract. Fortunately many digestive disorders are relatively minor—an upset stomach or a touch of gas. These conditions usually go away by themselves or, if they become too uncomfortable, can be treated with non-prescription, or over-the-counter, drugs. The ingredients in these products have been reviewed for safety and effectiveness by a number of panels of non-government experts assisting in FDA's massive review of OTC drugs.

There are, for instance, antacids that can be taken for an upset stomach associated with heartburn, sour stomach or acid indigestion. Simethicone can help relieve the symptoms of flatulence, or excess gas, according to FDA.

But another panel, in a recent report, has found no evidence that gas has anything to do with symptoms that occur in conditions called "immediate postprandial upper abdominal distress" (IPPUAD) and "intestinal distress" (ID). The group found no safe and effective ingredients in today's OTC products that will relieve IPPUAD symptoms of bloating, distention, fullness or pressure. This uncomfortable feeling develops within 30 minutes after eating. Nor did the panel find any safe and effective ingredients to relieve ID, a similar uncomfortable feeling that occurs 30 minutes to several hours after eating.

There are 100 or more diseases that can cause diarrhea, including viral and bacterial infections, diseases of the gastrointestinal tract, or various hormone and metabolic disturbances. What is experienced most frequently, however, is a mild, two-day illness sometimes associated with loss of appetite, abdominal cramps, nausea and vomiting, usually caused by an intestinal virus. Rest in bed, plenty of fluids and perhaps a drug such as

Except for the conscious act of chewing and swallowing, most people don't give much thought to the digestive process. It is completely automatic.

paregoric to reduce diarrhea and abdominal cramps are what's needed to treat mild cases. Diarrhea lasting more than two days should be treated by a physician.

On the opposite side of the coin, of course, is constipation. Simple constipation results most often from improper diet, inadequate fluid intake, possibly lack of exercise or a change in habits during travel. Laxatives can help get things moving again, but they should not be used too often. Overuse of laxatives can impair normal bowel function. Acute abdominal pain and vomiting could be symptoms of a serious condition such as appendicitis. Laxatives should never be used to treat such symptoms.

Much has been said about adding fiber to the diet to relieve constipation as well as a number of other bowel problems. Eating more whole grain breads, cereals, fruits and fresh vegetables can add bulk to the diet and that does help prevent constipation. However, too much fiber can have distressing side effects such as a feeling of being "stuffed" or "bloated." Large amounts of fiber also can impair the body's ability to absorb certain important minerals such as iron, copper and calcium.

Lack of dietary fiber and overuse of laxatives are thought to lead to hemorrhoids, that universal and much maligned condition of the nether end of the GI tract. Whether increasing the fiber in the diet does any good for hemorrhoids is a matter of conjecture, but there are a number of OTC products that will relieve pain and itching, reduce swelling and protect inflamed tissues.

Minor gastrointestinal upsets such as those described above are rarely serious, but there are some very serious, even life-threatening digestive diseases that are major health problems. According to the National Institute of Arthritis, Diabetes and Digestive and Kidney Diseases (NIADDK), some 20 million Americans are chronically ill due to digestive disease and more people are hospitalized because of these conditions than for any other group of disorders. The economic cost is enormous: $17 billion yearly in medical care, $35 billion in lost wages. Approximately 200,000 deaths a year are attributed to digestive diseases.

Among the major digestive diseases are hiatal hernia, peptic ulcer, cirrhosis of the liver, gallstones, Crohn's disease, ulcerative colitis and diverticulitis.

A hernia is the protrusion of an organ through a wall of the cavity in which it is enclosed. In the case of a hiatal hernia, it is the stomach that protrudes and the hole through which it goes is a teardrop-shaped opening in the diaphragm where the esophagus and stomach join.

Hiatal hernia may develop in people of all ages and both sexes, although it is considered to be a condition of middle age. The most frequent cause is an increased pressure in the abdominal cavity produced by coughing, vomiting, straining at stool or sudden physical exertion. Pregnancy, obesity or excess fluid in the abdomen also contribute to causing this condition. The hernia itself is painless. What brings the patient to the doctor is heartburn and indigestion caused by esophagitis, an irritation of the esophagus from stomach acid that is often, but not always, associated with hiatal hernia.

Most hiatal hernias do not need treatment. However, if the hernia is complicated by esophagitis, treatment is necessary because ulceration and scarring of the esophagus may eventually develop, making it impossible for the patient to swallow food. Most cases respond to antacids, bland diet, weight reduction and common sense about eating, drinking and other living habits. If symptoms persist, surgery can restore the stomach to its proper position and strengthen the area around the opening.

A peptic ulcer is a crater-like sore in the lining of the esophagus, stomach or duodenum, i.e., those areas bathed by the acid and pepsin in the digestive juices. The action of the acid on the sore place is what causes the pain. Duodenal ulcer occurs eight times more often than stomach or gastric ulcer. Why this is so is not fully understood. Anxiety, stress, alcohol, coffee and aspirin can stimulate the flow of gastric acid even when there is no food in the stomach.

The most common symptom of duodenal ulcers is a steady gnawing or burning pain in a small area of the abdomen between the navel and lower end of the breast bone. This pain usually starts within 30 minutes to 2 hours after eating and can usually be relieved by eating more food or by taking antacids. Ulcer treatment is aimed at reducing the amount of acid or irritants in the stomach. Drugs such as antacids are used to neutralize the acid. Atropine or related drugs block nervous stimulation of stomach acid secretion. Cimetidine (Tagamet), in 1981 the No. 1 selling prescription drug in the nation, blocks the response to histamine, a chemical in the body that is a powerful stimulator of gastric acid. FDA recently approved a new drug, sucralfate (Carafate) that acts by forming a protective coating over the ulcer, preventing the digestive action of acid and pepsin.

Cirrhosis of the liver is a degenerative disease in which liver cells are damaged and replaced by scar tissue. When normal tissue is lost, the organ can't carry on some of its important

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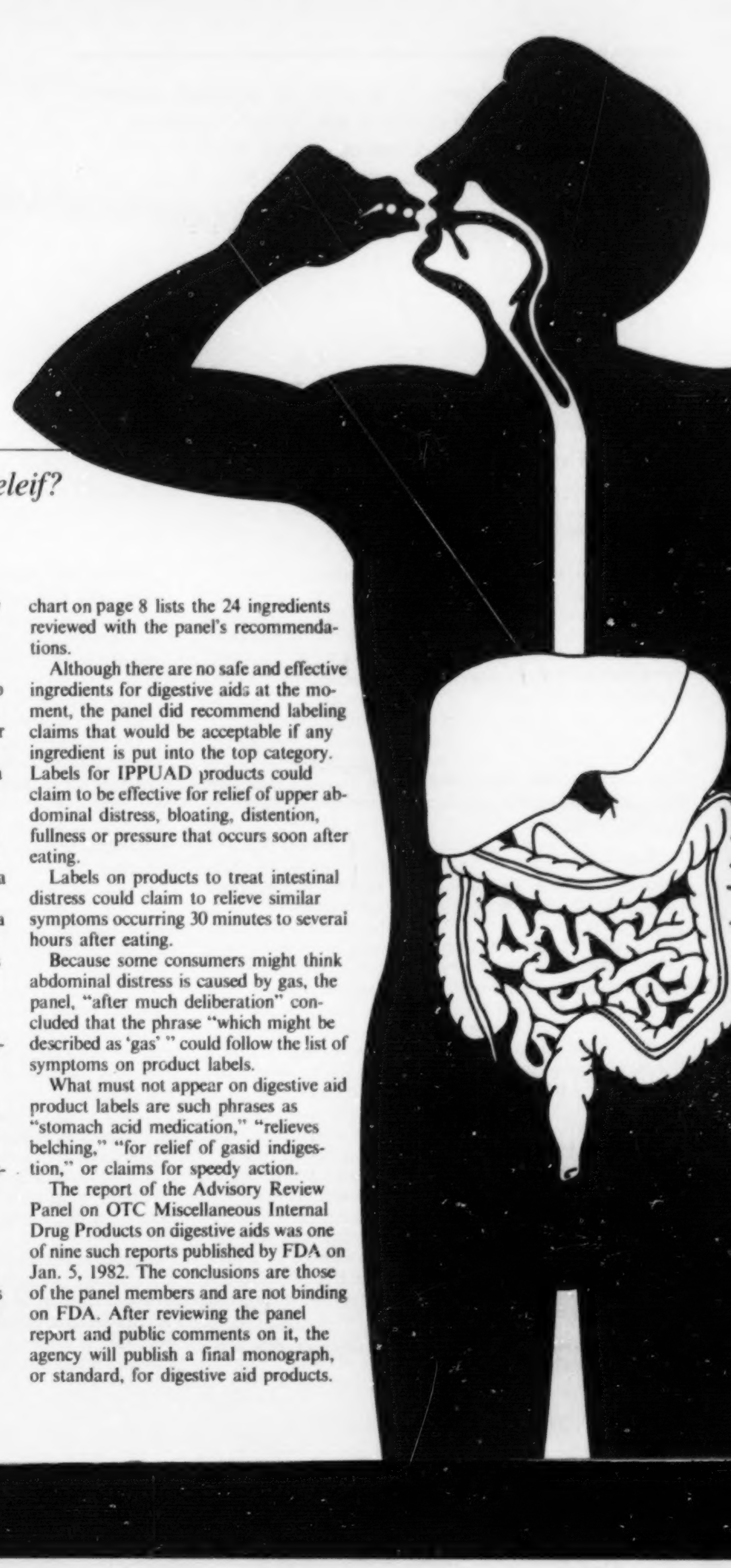


How Do Experts Spell Releif?

Excess gas in the GI tract, marked by belching, tummy rumblings and flatus (gas passed through the rectum) is probably more of an embarrassment than a medical problem. In fact there is no evidence that gas has anything to do with symptoms such as bloating, distention or fullness that occur in the abdomen after eating, according to a recent report by a panel of non-government experts studying over-the-counter digestive aids.

The panel, one of several assisting in FDA's massive review of OTC drug ingredients, looked at, but didn't review, a number of "anti-flatulent" ingredients because it found no evidence that gas is a cause of upper GI distress. None of the 24 ingredients the group did review was considered safe and effective for treating symptoms of what the panel called immediate postprandial upper abdominal distress (IPPUAD) or for a similar condition called intestinal distress (ID). Both conditions have basically the same symptoms: bloating, distention, fullness or pressure with abdominal discomfort. IPPUAD occurs immediately (within 30 minutes) after eating, while intestinal distress comes on 30 minutes to several hours after eating.

Dehydrated garlic, ox bile extract, pepsin and sorbitol are among the ingredients the panel said have no place in digestive aid products. Other ingredients such as aluminum hydroxide, activated charcoal, peppermint oil and sodium citrate need further testing to establish their effectiveness, the panel said. The chart on page 8 lists the 24 ingredients reviewed with the panel's recommendations.

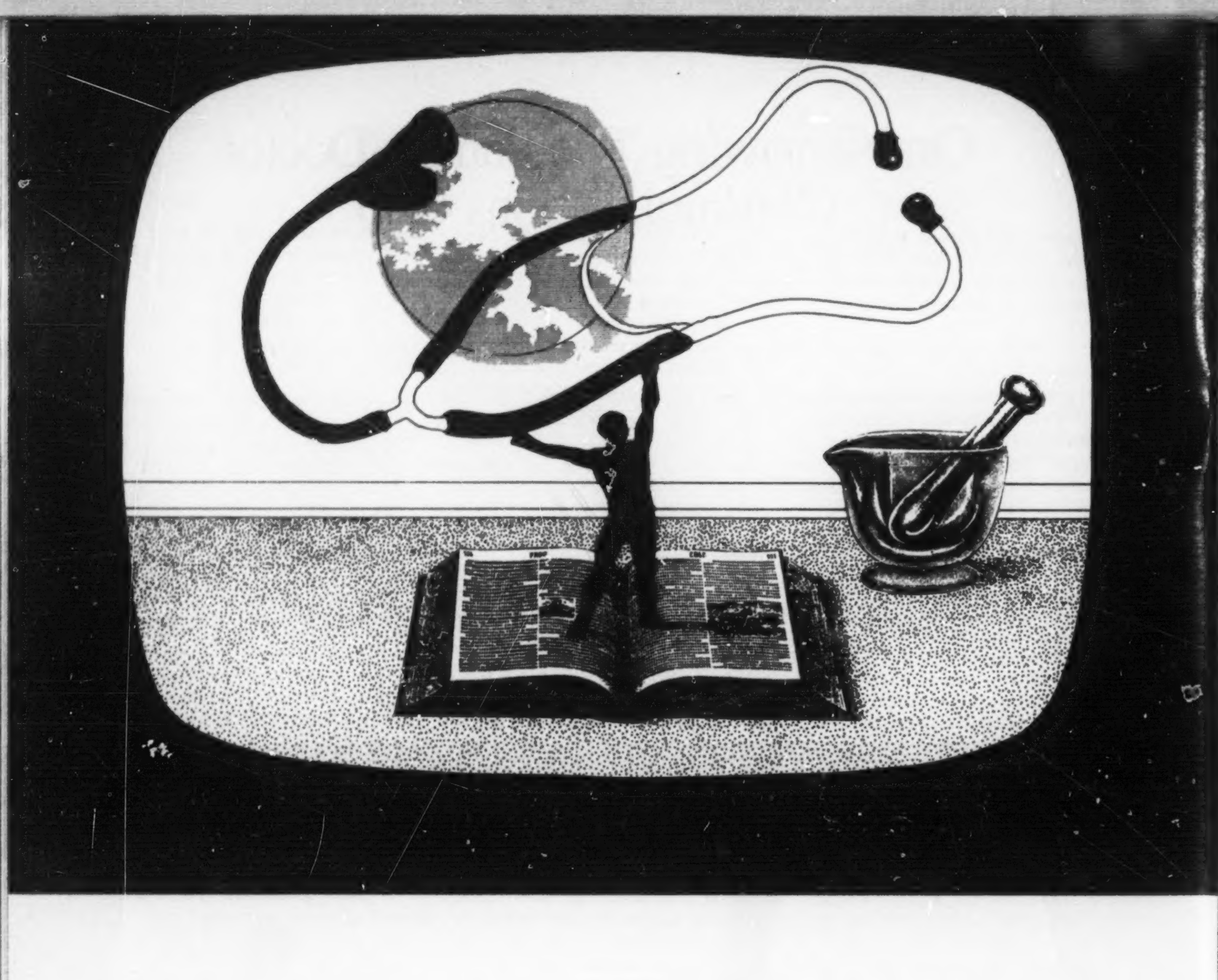
Although there are no safe and effective ingredients for digestive aids at the moment, the panel did recommend labeling claims that would be acceptable if any ingredient is put into the top category. Labels for IPPUAD products could claim to be effective for relief of upper abdominal distress, bloating, distention, fullness or pressure that occurs soon after eating.

Labels on products to treat intestinal distress could claim to relieve similar symptoms occurring 30 minutes to several hours after eating.

Because some consumers might think abdominal distress is caused by gas, the panel, "after much deliberation" concluded that the phrase "which might be described as 'gas' " could follow the list of symptoms on product labels.

What must not appear on digestive aid product labels are such phrases as "stomach acid medication," "relieves belching," "for relief of gasid indigestion," or claims for speedy action.

The report of the Advisory Review Panel on OTC Miscellaneous Internal Drug Products on digestive aids was one of nine such reports published by FDA on Jan. 5, 1982. The conclusions are those of the panel members and are not binding on FDA. After reviewing the panel report and public comments on it, the agency will publish a final monograph, or standard, for digestive aid products.



program was stayed last year by FDA Commissioner Arthur Hull Hayes Jr., and FDA proposed to withdraw it in December 1981.

While that proposal was being commented on, Hayes set up a special group to coordinate government and industry plans for providing the public with information on drugs. Given a proper government name—Committee on Patient Education—that could be made into an acronym, COPE, the group set to work. Ideas poured forth.

Two proposals from outside government drew particular interest. Both are seven-figure projects. One is from Ciba-Geigy, a major pharmaceutical manufacturer, and the other from the American Medical Association.

Ciba-Geigy plans to spend a million dollars in the next few years to encourage a dialogue between patients and doctors/pharmacists about prescribed drugs. The firm's plans include radio and television public service announcements and other advertisements. Ciba-Geigy also proposes to join in a consortium of health, industry and consumer groups for long-range work on patient education.

Said Ciba-Geigy in its presentation to the FDA committee:

"Patients have not gotten the information that they need because they have not asked for it and because their physician or pharmacist has not been willing to provide it."

The firm's $1 million expenditure would go for staff salaries, meeting expenses and other costs associated with the proposed Joint Commission on Patient Education, as well as for advertising.

The headline for the proposed print advertisements offered by Ciba-Geigy says:

"Even miracle drugs can't work unless they're used properly."

The ads are designed for both consumer publications and professional journals.

The American Medical Association's program calls for the distribution of preprinted prescription pads to physicians. Printed on the pads would be drug information, including side effects. The doctor would merely fill in the name of the patient, the generic or brand drug name, any special instructions and the dosage.

The information to be preprinted on the pads would be based on information used by the United States Pharmacopeia in its book, *About Your Medicines*. The leaflets are aimed at an eighth grade reading level. The 5½ by 8½-inch pads, costing about $2 each, would contain 100 such forms. The AMA plans call for spending $2 million on the program. That would include advertising campaigns designed to encourage physicians to use the pads and to familiarize the public with the program.

The program was pretested with 1,400 physicians. Patients should be seeing the first of the forms by September. A radio and television public service announcement campaign will accompany the introduction. In those ads, the public will be encouraged to ask for the preprinted forms.

The first pads will cover the 20 most widely prescribed drugs. AMA is considering sending sample forms to all of its 440,000 members. The association will also use conventional medical media and will work through state and county medical societies and specialty societies to persuade physicians to use the forms.

The United States Pharmacopeia is an independent, non-profit corporation that sets the official standards of strength, quality, purity, packaging and labeling for medical products used in this country. The USP dispensing information system includes brochures, posters, promotion packages, advertisements, books and newspaper columns aimed at professionals and patients. The items may be purchased from USP, although of course the monthly newspaper column is distributed free to some 700 publications. Many of the publications are in Spanish and others are slated to be translated into other languages.

The USP book, *About Your Medicines*, is available in many pharmacies and may be found in bookstores as *The Physician's and Pharmacist's Guide to Medicines*.

These projects are just a few of the exploding list of information items available about prescription drugs. Many pharmacies now have books near the prescription counter for customers to consult, and commercial bookstores are filled with books on prescription drugs.

It's obvious that the patient is no longer expected to hold his tongue and check his curiosity when medicines are involved. In fact, in the new relationship the health professional is expected to be anxious to satisfy the patient's right to know about that strange chemical that he is expected to put inside him.

Proposed Television Spot:

Following is the transcript of a proposed television public service announcement prepared by Ciba-Geigy, a major pharmaceutical manufacturer, as part of the firm's proposed $1 million effort to educate the public on drugs:

Video	**Audio**
Female patient talking to doctor. Doctor hands patient prescription.	*DOCTOR: All right, Mrs. Mason. We'll see you again in a month. Here's a prescription I want you to take.*
Freeze frame and split screen, hold doctor and patient on ieft.	*ANNOUNCER: Hold it!*
Pop in pharmacist and male customer right of screen. Pharmacist hands prescription to customer.	*PHARMACIST: Your prescription's ready, Harry.*
Freeze frame, holding both scenes.	*ANNOUNCER: Hold it. Right now, there's something both of you should be doing.*
Alternate casual footage from both scenes of patients talking to doctor and pharmacist.	*ANNOUNCER: You should be asking your doctor and pharmacist about the medication that's been prescribed for you. What kind of questions? Well, be sure you understand just how to take it. If directions say twice-a-day, does that mean when you get up and when you go to bed? Or, with breakfast and dinner? Are there any foods you should avoid while taking the medication? What about alcohol? What side effects might you experience? Should you stop taking the medicine if you feel better . . . or keep on taking it as prescribed?*
Dissolve logo and super "The more you know about the medicines you take the better they'll serve your health."	*ANNOUNCER: Your doctor or pharmacist will give you clear, easy-to-understand information. Ask for it. Remember the more you know about the medicines you take, the better they'll serve your health.*

Fortunately many digestive disorders are relatively minor — an upset stomach or a touch of gas. These conditions usually go away by themselves or, if they become too uncomfortable, can be treated with non-prescription, or over-the-counter, drugs.

How The Panel Rated Digestive Aid Ingredients

Ingredient	Immediate postprandial abdominal distress	Intestinal distress
Almadrate sulfate	■	
Aluminum hydroxide	■	
Bismuth sodium tartrate		●
Calcium carbonate	■	
Cellulase	●	■
Charcoal, activated and charcoal, wood		■
Dehydrocholic acid	●	●
Dihydroxyaluminum sodium carbonate	■	
Duodenal substance		●
Garlic, dehydrated	●	●
Glutamic acid hydrochloride	●	●
Hemicellulase		■
Homatropine methylbromide	●	■
Magnesium hydroxide	■	■
Magnesium trisilicate	■	
Ox bile extract	●	●
Pancreatin and pancrelipase	●	■
Papain		●
Peppermint oil	■	
Pepsin	●	●
Simethicone	■	■
Sodium bicarbonate	■	■
Sodium citrate	■	■
Sorbitol	●	●

Category ■ —Further testing needed to establish safety and effectiveness
Category ● —Not safe and effective

work such as processing and disposal of nutrients, hormones, drugs and toxins.

Chronic alcoholism is the most common cause of cirrhosis in the United States, but the disease may also result from hepatitis, other viruses, some chemicals and poisons, an excess of iron or copper in the system, or obstruction of the bile duct. The onset of the disease may be "silent," symptoms not appearing until the disease is far advanced. The patient may experience fatigue, weakness and exhaustion, loss of appetite and weight, jaundice, intense itching, abdominal distention and copious hemorrhage from rupture of dilated veins in the esophagus.

Treatment depends on the type and stage of the cirrhosis and may include a strict diet, diuretics to decrease fluid retention, vitamins and, naturally, avoidance of alcohol. In some cases, surgery may be required to deal with the complications.

Gallstones are formed by aggregation of cholesterol, bile pigment, or calcium, or combinations of these, in the gallbladder. Their size can range from that of a pin head to a golf ball. When these stones get stuck in the bile ducts leading to the duodenum, the gallbladder and the duct try to dislodge them by muscular contractions, thereby causing severe abdominal pain. Blockage of the duct prevents flow of bile to the intestines and causes bile to back up in the bloodstream.

Gallstones are more common in people over 40, particularly in women and the obese. Surgery to remove the gallbladder is the traditional treatment for gallstones. Experimental drugs now being tested might prove effective in dissolving gallstones.

Crohn's disease and ulcerative colitis are two severe diseases of the intestines that have many things in common. The cause of neither is known and each tends to occur most often in young people and to run in families. Neither is contagious. Both diseases can produce ailments outside the intestines such as skin changes, arthritis and eye inflammation.

Crohn's disease affects both the small and large intestines and is characterized by a thickening and inflammation of all layers of the intestinal wall. Since sections of diseased bowel often occur between normal sections, the disease is sometimes called regional enteritis. When the colon is the site of disease it's called granulomatous colitis.

Symptoms of the disease may include anemia, abdominal pain, bloating, fever, diarrhea and malnutrition. Long hospitalization is common. Surgery may be required to remove diseased sections of the bowel, but the disease tends to recur in the remaining bowel. A long-term study sponsored by NIADDK has found sulfasalazine and prednisone to be effective in inducing remissions in some cases, but not in preventing exacerbation (increase in severity) of the disease.

Ulcerative colitis is an inflammation of all or part of the colon, or large bowel. The most common symptoms are abdominal cramps and bloody diarrhea. There also may be weight loss, anemia and loss of body fluids and minerals.

In general, treatment of ulcerative colitis is aimed at correcting malnutrition and halting the constant loss of blood, fluids and mineral salts. This calls for administration of intravenous fluids, or certain steroid drugs and antibiotics. Sulfasalazine may be prescribed over a long period to control symptoms and prevent recurrent attacks. In some severe cases surgical removal of the colon may be necessary.

Some scientists believe the Western diet of refined foods leads to diverticulosis—sac-like pouchings in the colon. Although most people with diverticulosis notice no symptoms or complications, about 15 percent develop an inflammation called diverticulitis. This occurs more often in men than women and more often on the left side of the body than on the right.

The symptoms are like those of appendicitis or colon cancer—crampy or steady pain and local tenderness. Many attacks are mild and pass without treatment. In other cases there may be a rupture of the pouches into the abdominal cavity with a small amount of bleeding. Heavy bleeding from erosion of a large blood vessel may occur, but is uncommon. Inflammation can produce abscesses and fistulas, that is, abnormal pathways into other nearby organs, or can lead to a narrowing of the colon with partial or complete obstruction of the channel.

Medical treatment of acute diverticulitis involves putting the colon "at rest"—that is, the patient takes no food by mouth. Antibiotics are given to fight infection. Surgery may be required in chronic cases. At one time, it was thought that a bland diet was the way to treat diverticulosis, but now doctors tend to agree that more bulk is what is needed.

There are, of course, many other digestive disorders, some caused by infectious diseases, others by parasites. Inborn errors of metabolism can interfere with the proper absorption of certain foods. The condition of the teeth and the state of emotions also can have an effect on the digestive system. Cancer can develop almost anywhere along that 30-foot route.

Automatic as it may be, the digestive system is not something to be taken for granted.

Annabel Hecht is a member of FDA's public affairs staff.

When Carp Was Dressed Up Like Tuna

About 75 miles southwest of Minneapolis is the town of Mankato, surrounded as are many towns in Minnesota by a dozen or so lakes, large and small.

Some people in Mankato may remember the Lakefish Canning Co. It operated there in the 1940s, putting up mostly carp taken from the nearby lakes.

Carp is an edible freshwater fish with a whitish, non-oily meat that tends to be flaky instead of firm. It is prized in many parts of the world, especially the Orient and Middle East, where it is raised in ponds for food. (See "They're Growing Food Under Water," in the Nov. 1981 *FDA Consumer.)* The classic Japanese kite, shaped like a fish, represents the carp.

But carp is not so highly thought of in the United States. Some people call it a "trash fish," and when lakes are cleared of undesirable fish, there is likely to be a great haul of carp, which are usually ground up for fertilizer.

Lakefish Canning apparently had a problem marketing its canned carp, particularly those cans whose labels told truthfully what was inside: "freshwater carp, packed in soya oil." On the back of the labels when peeled off were suggested recipes: a "super sandwich spread" when mixed with hard boiled eggs and mayonnaise; a "quick and good salad" when mixed with lettuce, tomatoes, dressing and hard boiled eggs.

But the company also did a bit of hedging some of the time. Some cans were labeled "lakefish." There is, of course, no fish species by that name, and one would not be far amiss to surmise that they contained carp, which after all did come out of the lakes. The recipe on these labels was for creamed lakefish, including a white sauce, mushrooms and hard boiled egg. "Lakefish can be used in any recipe that calls for tuna, boned chicken or turkey," boasted the label.

Such labeling apparently won Lakefish Canning few converts because it went bankrupt in 1950. The company's stock of canned carp and lakefish was purchased by the Price Wholesale Grocery Co. of St. Paul, a firm that specialized in buying "distressed merchandise."

The owner of the grocery firm was ill at the time the Lakefish canned products were being bought, and for two months his son Norman operated the business.

Perhaps Norman had been reading the backs of the labels, where it said in effect that canned carp is as good as tuna. At any rate, he decided to call it tuna, which sells for considerably more than carp.

Labels were printed by an Illinois firm. One set, marked "LC light meat tuna," showed a tuna leaping, perhaps out of a Minnesota lake. The cans, the label said, were packed for the LC Mercantile Co. of Quincy, Ill. The other set, marked "Veteran light meat tuna fish," showed a tuna not leaping. It was supposedly packed for the Gordon-Brewster Co. of Rochester, N.Y.

Carried along by the idea, Norman and two friends removed the labels from 22,320 cans and replaced them with LC and Veteran labels. Then Norman shipped out the carp-turned-tuna.

The venture quickly fell apart. A housewife in Minneapolis doubted it was tuna, and expressed her doubts to the FDA district office in that city. The district assigned Hugh J. Hennessey, an experienced FDA investigator, to the case. Assisted by FDA's Chicago office, Hennessey determined that LC Mercantile was a fictitious firm, as was Gordon-Brewster.

Working back through retail stores in the Minneapolis-St. Paul area, Hennessey patiently traced the relabeled carp to Price wholesalers. For some time Norman claimed that the distressed merchandise he had bought came with the false labels on it.

But that story did not hold up. Hennessey, aided by Minnesota investigators, reconstructed the events that had happened. Norman admitted his offense and turned over his distribution records to the investigators.

These records showed that Price wholesalers had received 465 cartons of canned carp when Lakefish Canning went bankrupt. They showed that 423 of these cartons (now labeled tuna) had been sold to retail outlets. Some of the cans had in turn been sold to consumers, and their contents presumably eaten.

It should be noted that the product was not harmful. In fact, it was a perfectly good can of fish, but it was carp, not tuna. The deception was in the labeling.

Retailers who had bought the mislabeled carp were reimbursed by Price wholesalers. The company and Norman were fined, and 200 unsold cartons, some at Price wholesalers and some in retail stores, were seized by court order. Since the contents were wholesome, even if not toothsome, the cans were donated by the court to charitable institutions.

But the story didn't end there. The entire sequence of events became an FDA classic account of economic fraud, in which the culprits were brought to justice and only the orphanages benefitted.

For a decade after this 1951 case, five cans from the Lakefish episode were used by Wallace Janssen, formerly FDA's information officer and now the agency's historian, in appearances before lecture audiences. The cans showed the labeling and relabeling progression from carp or lakefish to tuna. Janssen calls it one of his best ever show-and-tell road shows. One can (the LC tuna) bore Investigator Hennessey's scribbled name, the date he obtained it as evidence (4-19-51) and the sample number.

The five cans were retired to a storage shelf in the 1960s and kept by Janssen among other FDA relics. In the mid-1970s, Janssen moved his office and left the cans with another agency employee. By then they were a quarter of a century old and were beginning to swell and bulge. A photo was made of them then, at age 25, and they were returned to their box on the shelf.

In 1981 they were taken out, 30 years from the time Hennessey scribbled his name on the one can. Two cans, fairly flat five years earlier, were bulging from gaseous buildup, and three that had been swollen at the time now appeared about to burst. They were obviously ready to be retired, but one more use was found for them: They were offered to FDA's Bureau of Foods for laboratory analysis.

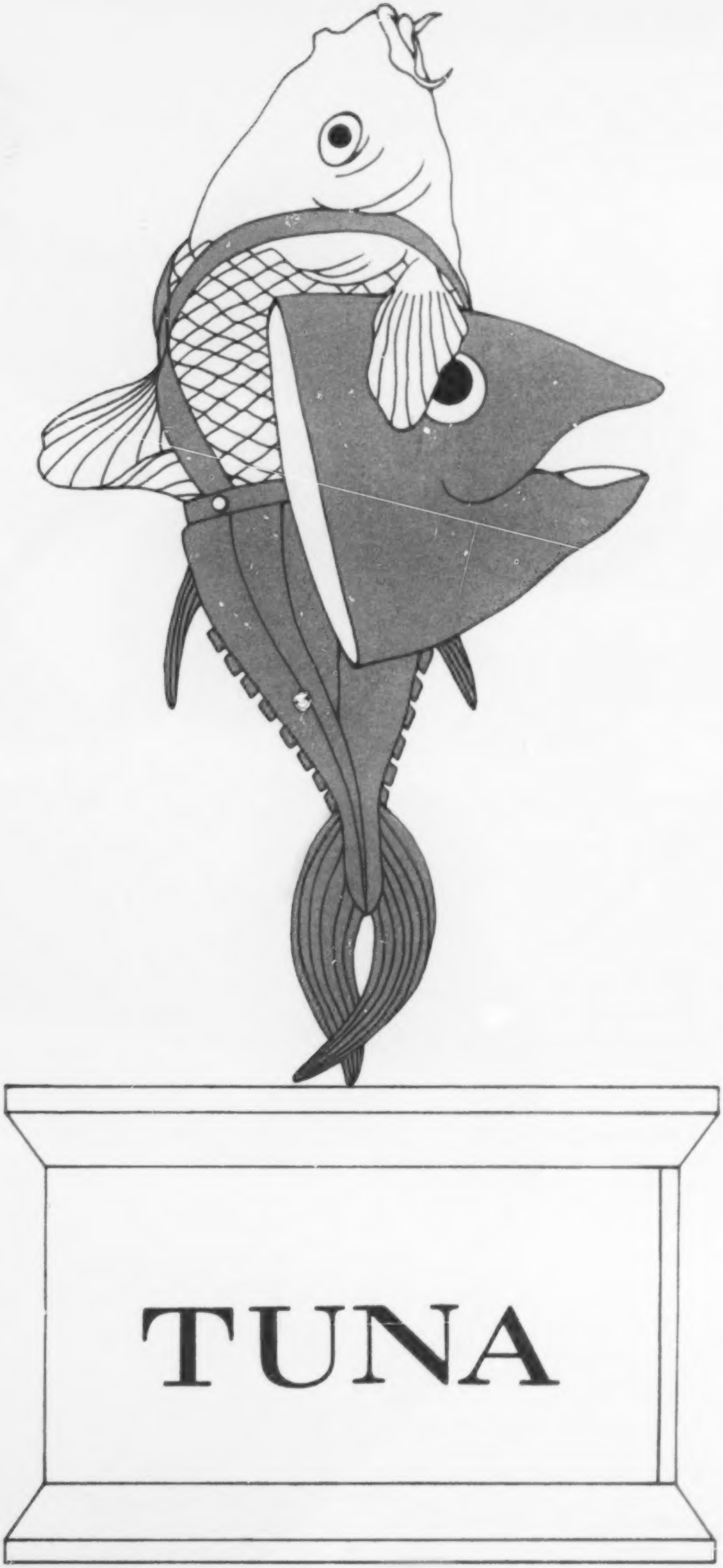
In January 1982 an FDA scientist gingerly peeled off the labels. On the back were the recipes from 30 years before. One by one the cans were carefully punctured under a shielded laboratory hood. Two cans had so corroded from the inside that the gases exploded through the puncture holes.

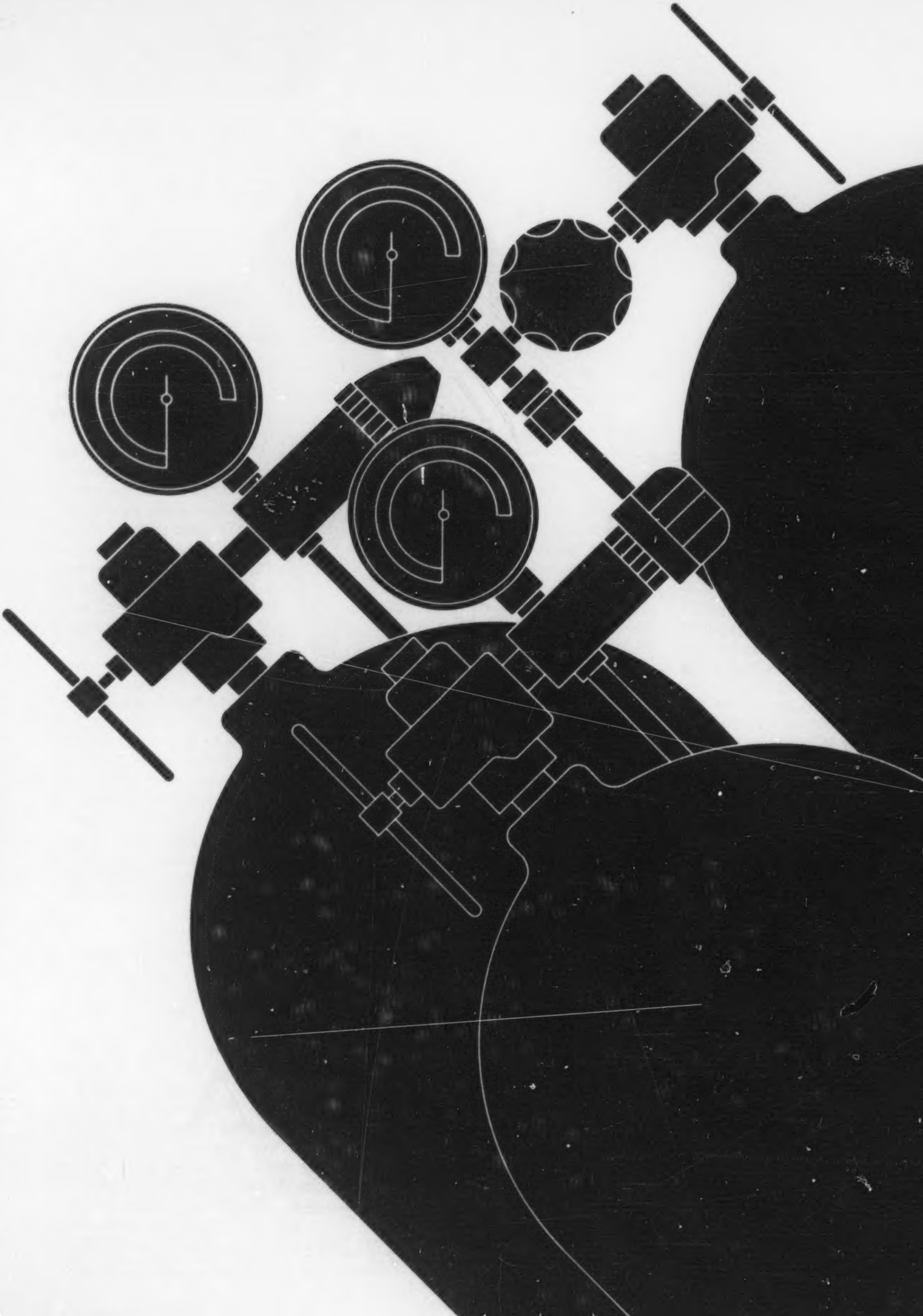
"The cans of fish are the oldest such samples we have examined," the scientist wrote in his report, "yet the contents are in surprisingly good condition. There was some deterioration but no advanced spoilage, even after 30 years. There are off odors, and the general appearance of the contents is not appealing, due in part to flaking of the can coating and uneven blackening of the metal surface. But there is no decomposition, which illustrates the extended periods of storage that fish properly packed can undergo."

In a footnote the scientist added, "The cans labeled tuna did contain carp, and I doubt that anyone could be deceived into thinking otherwise."

Did you hear that, Norman?

—Richard Thompson





Gases Are Drugs, Too

by Richard C. Thompson

Question: When is a drug not in tablet, liquid, ointment or capsule form?

Answer: When it is a gas.

There are 200 or so compressed gases produced and used in the United States, ranging from acetylene to vinyl ether. Ten of these are used as "medical gases."

The 10 are regulated as drugs through labeling under the Food, Drug, and Cosmetic Act. They're considered drugs because they meet the act's definition of being substances intended for prevention, diagnosis or treatment of disease, and affecting the structure or function of the body.

Listed alphabetically, the medical gases are air, carbon dioxide, carbon dioxide-oxygen, cyclopropane, helium, helium-oxygen, nitrogen, nitrous oxide, oxygen and oxygen-nitrogen.

It may not be apparent, but the list begins with air and ends with air.

The first is the ordinary Earth atmosphere that everyone breathes. It may become too contaminated with pollutants to be called "pure" by FDA standards when it is compressed from the atmosphere and put into a tank for medical uses. So instead an oxygen-nitrogen mixture, a manufactured air, may be in the tank, with the right proportions of the two gases. In fact, it is often less expensive to mix oxygen and nitrogen to get an acceptable air than to filter out pollutants from atmospheric air.

FDA's Bureau of Drugs has the prime responsibility for assuring the safety and effectiveness of medical gases, just as it does for all drugs. Since the gases may also be used to treat animals, the Bureau of Veterinary Medicine has an interest too.

Although very important to the health and medical professions and to the public, medical gases constitute a fairly small segment of the huge compressed gas industry in the United States.

That industry supplies compressed gases (even in liquid form they are called "compressed") to almost every manufacturing and processing industry in the country: fertilizers (anhydrous ammonia) for farming, propane for heat, acetylene for metal working, carbon dioxide for fire extinguishers, neon for lighting, fluorocarbons for refrigerants, chlorine for water purification and nitrous oxide for pressurized consumer products such as paints, shampoos and insecticides. This list of uses for these compressed gases, by themselves or in combination, is almost endless.

The compressed gas industry as a whole is regulated by the Department of Transportation to ensure the safe movement throughout the country of what are clearly dangerous and often explosive substances—gases under pressure. The DOT regulations cover the entire spectrum of compressed and liquefied gas manufacture, transport and storage.

In June 1981, FDA's Division of Drug Manufacturing issued guidelines that specify the practices and procedures acceptable to FDA to satisfy the regulations. Close production controls and accurate record keeping are required of the 425 gas manufacturers registered with the agency.

The DOT rules apply to all compressed gases, including the 10 medical gases. FDA regulations incorporate these requirements as they concern shipping and storage, but the agency applies additional rules for gases with medical uses.

It should be noted that gases become medical gases only because of the intended use. A cylinder of oxygen for medical use, for example, was produced no differently than the one for industrial use. It likely came off the same production line or filling manifold and from the same bulk tank. But the FDA layer of regulation over the basic DOT regulations is added insurance that the medical gas will be what it should be.

All of the medical gases or gas combinations have industrial uses. In fact, the primary use is in manufacturing and industry. That they are medical gases is almost incidental.

Described in alphabetical order, here are the medical gases, and specifications and labeling requirements for them:

- Air is a colorless, odorless mixture of nitrogen and oxygen, with the oxygen content ranging between 19.5 percent to 23.5 percent. Air is essential to and will support life. It is non-flammable but does support combustion. It is made by compressing dried and purified atmospheric air or by mixing nitrogen and oxygen. It is administered whenever a patient needs simple atmospheric air, perhaps under positive pressure for lung ventilation. Tanks containing air must be painted yellow.
- Carbon dioxide (CO_2) is a pungent, colorless gas that will not support life. It is non-flammable and will not support combustion. CO_2 occurs naturally in springs of carbonated water (formed by the action of earth acids on limestone) and is manufactured commercially by thermal decomposition of carbonate. It is used in laboratory tests, to check patient respiratory response and to test lung function following surgery. Tanks containing CO_2 must be painted gray.
- Carbon dioxide-oxygen combinations are mixtures of the two gases, ranging from 1 percent CO_2 and 99 percent O_2 to 30 percent CO_2 and 70 percent O_2. The mixtures are used medically for diagnosis (usually, lung function tests) and for inhalation therapy. Tanks containing CO_2-O_2 combinations must be painted gray and green.
- Cyclopropane (C_3H_6) is a colorless gas with a characteristic odor. It is a strong anesthetic that will not support life and is highly flammable. It is used rarely now as an inhaled anesthetic. Tanks containing the gas (which is liquefied in the tank but comes out as a vapor) must be painted orange.
- Helium (He) is an odorless, colorless gas that will not support life. It is non-flammable and does not support combustion. Helium is made from liquefied, purified natural gas. It is used medically in laboratory analysis and in combination with oxygen. Tanks containing helium must be painted brown.
- Helium-oxygen combinations are supplied in various mixtures, the most common being 80 percent helium and 20 percent oxygen. Mixtures of more than 80 percent helium may not support life. It is used medically for diagnostic tests and in inhalation (breathing) therapy. Tanks containing helium-oxygen mixtures must be painted brown and green.
- Nitrogen (N_2) is a colorless, odorless gas that will not support life. Non-flammable, it will not support combustion. The usual method for manufacturing nitrogen is through separation from atmospheric air. It is used medically for diagnostic testing and for inhalation therapy. Tanks containing nitrogen must be painted black.
- Nitrous oxide (N_2O) is a colorless, odorless anesthetic that will not support life. Below 98 degrees F and under pressure (as it would be in a tank) it is usually a liquefied gas that vaporizes when it is released. It is non-flammable but does support combustion. It is used medically (with oxygen) as an anesthetic and pain-killing (analgesic) drug. Tanks containing N_2O must be painted blue.
- Oxygen (O_2) is a colorless, odorless gas that will support life. It is non-flammable but supports combustion. It is manufactured by separation from dried, purified atmospheric air. It is used in medical emergencies, such as accidents and heart attacks; in short-term and long-term care of many chronic diseases; and as a necessary component of any inhaled anesthesia, given in the proportion (at least 20 percent) that it occurs in atmospheric air. Tanks containing oxygen must be painted green.

Each compressed medical gas must be properly labeled and meet the standard for that gas in the United States Pharmacopeia (USP). The USP officially defines and sets standards for chemicals and chemical compounds that have medical and pharmaceutical uses. These definitions are accepted by both industry and government agencies, particularly FDA, as being the official description or formula for that compound. A product that varies from those descriptions is in violation of the FD&C Act.

The USP was founded in 1820 to set such standards. As new chemical (drug) compounds are developed, the USP is updated through meetings of its members from the medical and scientific community. The adopted recommendations of these members are added to the USP and become the legal identities for those chemicals or compounds.

Both FDA and industry use the USP standards for medical gases. For example, the standards on helium tell the manufacturer that helium must be packed and stored in cylinders; that helium will give a small balloon decided buoyancy; that a burning splinter will be extinguished when inserted into an inverted test tube filled with helium (use caution); and that a certain specific gravity at a given pressure and temperature will indicate 99 percent helium.

USP also describes the odor test for helium: Carefully direct a small flow of gas (helium) from the slightly opened container (tank) valve toward the tester's nose; no appreciable odor should be detected.

The odor (sniff) test is used in the compressed gas industry to identify the fumes or gases that may be in a tank or container. It is done as the USP describes it for medical gases: a slightly opened valve and a quick sniff of the tank's contents. A gas industry handbook cautions against doing this with anesthetic gases and advises never to release it directly into the tester's face.

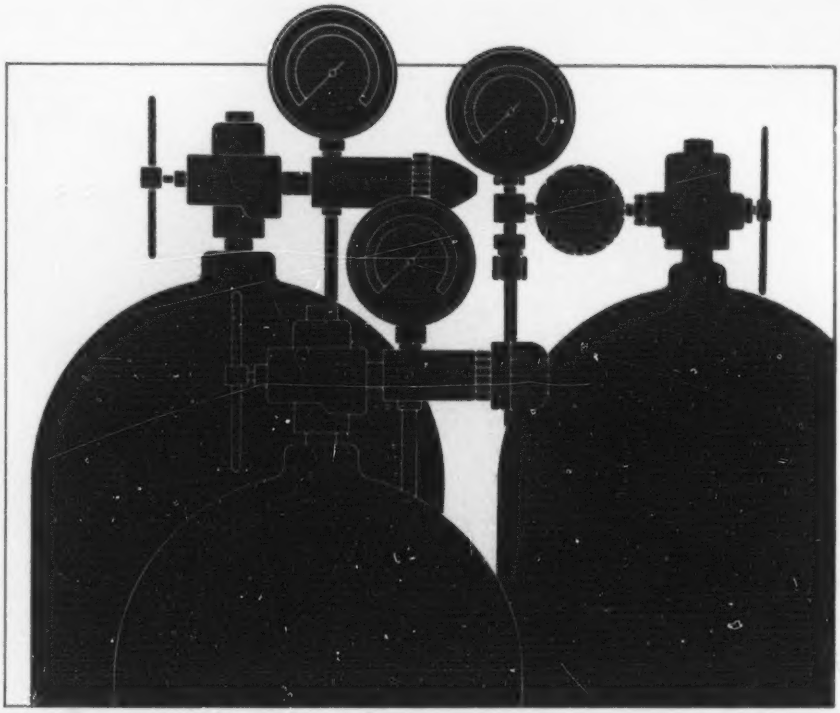
Another basic test described by the compressed gas handbook determines the soundness of a tank or container. It is as simple and direct as the sniff test and is done with a hammer struck against the side of the tank. A tank that is in good condition will produce a clear, bell-like ring; one that is defective, and therefore should be discarded, will produce a dull thud.

Errors in handling of medical gases are rare. When they do occur, it is likely to be filling a tank with the wrong gas (which seldom happens) or the wrong label on a tank, such as a nitrogen tank marked nitrous oxide. Since the nitrogen tank is black, and since users of these medical gases know the required colors, they will quickly learn what's in the tank and switch over to another tank if it's not nitrogen. Almost always the error will be in the label. These errors are reported to FDA by the hospital or other user, and the agency will inspect the filling plant that supplied the tank to prevent its happening again.

Errors sometimes occur in tank hookups too, although this is even rarer than putting the wrong gas in a cylinder. FDA requires that hose and valve connections have pin or thread arrangements that prevent medical gas cylinders from being mixed up in connecting.

Many hospitals have piped-in oxygen and other medical gas lines in their operating rooms and in patient rooms. Then all the nurse or anesthesiologist needs to do is connect the anesthesia mask or breathing apparatus to the wall connector and turn on the valve. The gas is supplied from banks of cylinders elsewhere or outside the hospital, or sometimes from a storage container of the gas in liquid form that becomes a vapor as it is dispensed in the hospital.

Richard C. Thompson is a member of FDA's public affairs staff.



How Pain Was Put To Sleep

"There will," read the poster, "be a Grand Exhibition at the Masonic Hall of the effects of inhaling the new LAUGHING GAS!

"Thirty gallons of GAS will be administered to all in the audience who wish to inhale it. Strong Men will be invited from the audience, to protect those under the influence from injuring themselves or others.

"The GAS will be administered only to Gentlemen of the first respectability. The effect is to make those who inhale it Laugh, Sing, Dance, Carry On or Fight, according to their character. Probably no one will attempt to fight.

"The Entertainment will be accompanied by experiments in ELECTRICITY!"

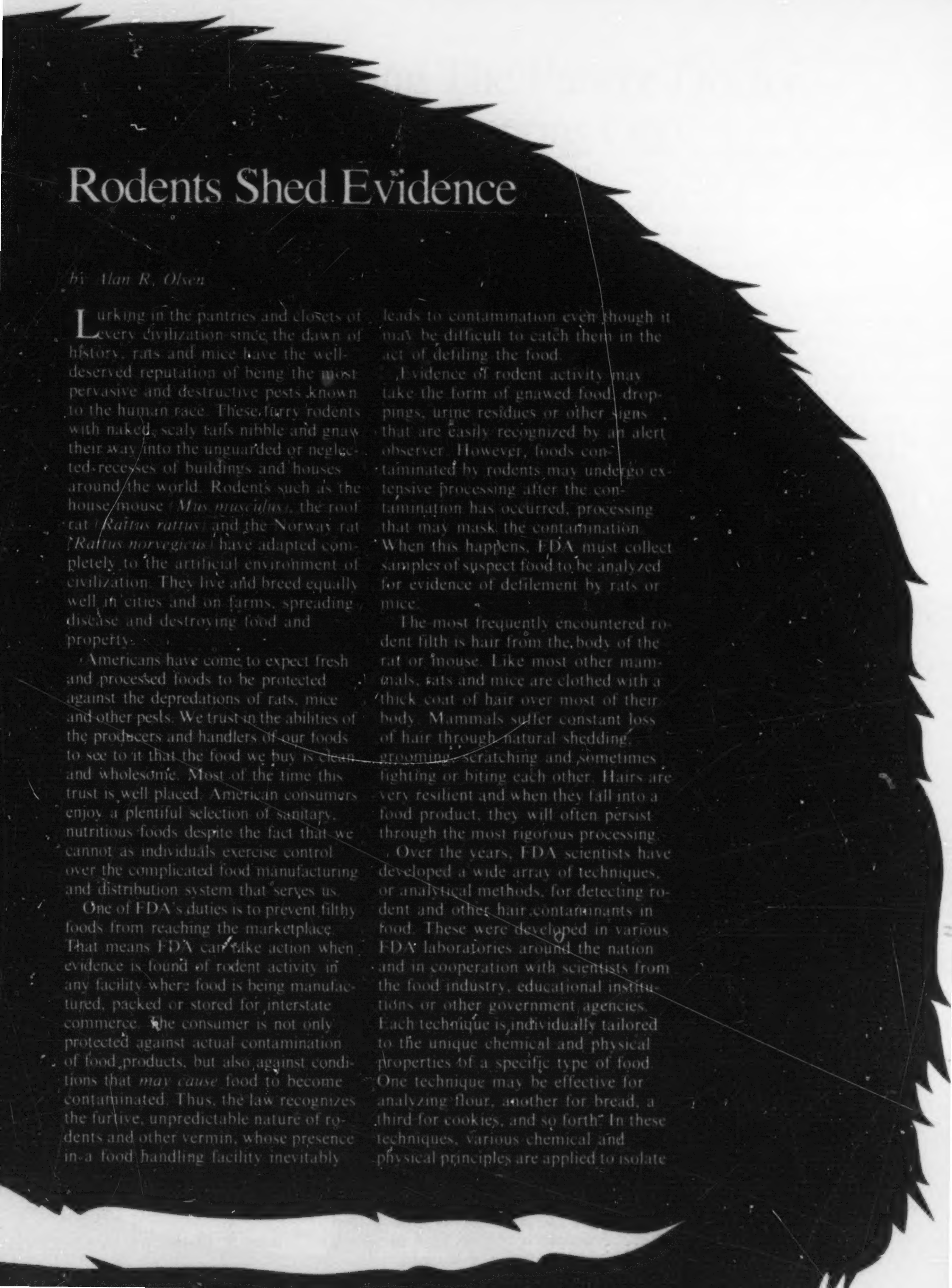
The year was 1843, the place a small town in the United States and the LAUGHING GAS was nitrous oxide, N_2O, a substance that deserved more than being An Entertainment.

That recognition came a year later when a Hartford, Conn., dentist, intrigued by the possibilities of this substance, extracted a molar from a patient under the influence of N_2O with no objections by the patient. Painless dentistry had arrived.

The surgical profession became interested in this new technique, since surgeons had to operate with the patient awake or a bit inebriated. A demonstration was set for Oct. 16, 1846, at Boston General Hospital. A chemist friend suggested to Dr. William Morton, who was arranging the event, that ether, a liquid that turns to gas at ordinary temperatures, be used instead of nitrous oxide. It was, and the surgeon removing the tumor from the unconscious patient was astounded. "Pain has been put to sleep," he supposedly said. Boston essayist Oliver Wendell Holmes named the technique "anesthesia."

Ether was used for over a century as a dental and surgical anesthetic, despite its being a dangerous, flammable, explosive substance. It changes easily from liquid to a heavier-than-air gaseous form that can be accidentally ignited by a spark some distance away.

Increased use of electrical equipment in hospitals since the 1950s has made ether unwelcome, and it is obsolete as an anesthetic in the United States. But it more than served its purpose by introducing the concept of anesthesia. Nitrous oxide, with which in a way it all began, is still an accepted medical (anesthetic) gas. It is also used as a propellant in aerosol pressure cans of whipped cream, cheese and other foods, and sometimes misused by persons who are seeking a "drug high." (See "Inhalants: Quick Route to Danger," *FDA Consumer*, May 1980.)



Rodents Shed Evidence

by Alan R. Olsen

Lurking in the pantries and closets of every civilization since the dawn of history, rats and mice have the well-deserved reputation of being the most pervasive and destructive pests known to the human race. These furry rodents with naked, scaly tails nibble and gnaw their way into the unguarded or neglected recesses of buildings and houses around the world. Rodents such as the house mouse (*Mus musculus*), the roof rat (*Rattus rattus*) and the Norway rat (*Rattus norvegicus*) have adapted completely to the artificial environment of civilization. They live and breed equally well in cities and on farms, spreading disease and destroying food and property.

Americans have come to expect fresh and processed foods to be protected against the depredations of rats, mice and other pests. We trust in the abilities of the producers and handlers of our foods to see to it that the food we buy is clean and wholesome. Most of the time this trust is well placed. American consumers enjoy a plentiful selection of sanitary, nutritious foods despite the fact that we cannot as individuals exercise control over the complicated food manufacturing and distribution system that serves us.

One of FDA's duties is to prevent filthy foods from reaching the marketplace. That means FDA can take action when evidence is found of rodent activity in any facility where food is being manufactured, packed or stored for interstate commerce. The consumer is not only protected against actual contamination of food products, but also against conditions that *may cause* food to become contaminated. Thus, the law recognizes the furtive, unpredictable nature of rodents and other vermin, whose presence in a food handling facility inevitably leads to contamination even though it may be difficult to catch them in the act of defiling the food.

Evidence of rodent activity may take the form of gnawed food, droppings, urine residues or other signs that are easily recognized by an alert observer. However, foods contaminated by rodents may undergo extensive processing after the contamination has occurred, processing that may mask the contamination. When this happens, FDA must collect samples of suspect food to be analyzed for evidence of defilement by rats or mice.

The most frequently encountered rodent filth is hair from the body of the rat or mouse. Like most other mammals, rats and mice are clothed with a thick coat of hair over most of their body. Mammals suffer constant loss of hair through natural shedding, grooming, scratching and sometimes fighting or biting each other. Hairs are very resilient and when they fall into a food product, they will often persist through the most rigorous processing.

Over the years, FDA scientists have developed a wide array of techniques, or analytical methods, for detecting rodent and other hair contaminants in food. These were developed in various FDA laboratories around the nation and in cooperation with scientists from the food industry, educational institutions or other government agencies. Each technique is individually tailored to the unique chemical and physical properties of a specific type of food. One technique may be effective for analyzing flour, another for bread, a third for cookies, and so forth. In these techniques, various chemical and physical principles are applied to isolate hairs from the contaminated product in which they have laid unseen. Some techniques are accurate enough to detect one hair in three pounds of food. Currently, over 100 of these techniques exist in FDA's analytical arsenal, and 5 to 10 new ones are added annually.

Examination of rodent and other hairs isolated from a food sample is performed by FDA microscopists who have been trained in the science of trichology, the study of hairs.

Since a single hair may be no wider than a strand of silk, it requires powerful microscopes to locate and study hairs even after the hairs have been isolated from a food product. A wide-field stereoscopic microscope is used to find, sort and measure hairs. This instrument is capable of producing three-dimensional images of hairs magnified up to 90 times actual size. At these magnifications, hairs are easy to recognize and can be counted and sorted into some basic categories. These categories include color, length and configuration such as straight, wavy, curly or twisted. Rodent hairs have a distinctive striated color pattern, consisting of thin alternating bands of black and clear areas along the length of the hair. Some rodent hairs may assume a characteristic wavy configuration with angular bends that is best described as "zig-zag."

With the wide-field microscope, the scientist can measure the lengths of hair contaminants found in a food sample to within one-tenth of a millimeter, a distance smaller than the diameter of the period at the end of this sentence. The length of a rodent hair may indicate, for example, whether a food product was exposed to rodents before or after a certain grinding process. Hairs present in the product prior to grinding would be broken into small fragments along with the food, while long hairs were probably introduced after grinding.

Still more powerful microscopes are needed to develop evidence concerning the identity of the rodent or other animal responsible for the contamination and the circumstances surrounding the contamination. For these purposes, a compound microscope that can magnify objects up to 1,000 times their actual size is used. This instrument can also shine a powerful beam of light completely through a hair specimen, enabling the microscopist to observe minute internal structures at the core of the hair. Also revealed by the compound microscope are patterns of scales (much like tiny fish scales) on the surface of the hair, small variations in width and the distribution of natural or dyed pigments.

Under the high magnifications of a compound microscope, soft fur hairs from a rodent's undercoat can be distinguished from the much coarser overhairs. In many cases, especially with rodents, the origin of a hair can be narrowed down to a specific body area such as the foot or the muzzle. By examining the root of a hair, the microscopist can often determine whether the hair was shed, pulled or cut from the hide of its owner. A compound microscope can even reveal whether the hairs went through the rodent's digestive system, having been swallowed by the rodent during grooming. Even if rodent droppings are crushed beyond recognition or dissolved, the evidence of hairs will usually survive to be discovered by an FDA microscopist.

To firmly establish the identity of a hair, it must be compared at high magnifications with various other reference hairs. Many FDA laboratories do this with a comparison microscope, a sophisticated instrument that mates two compound microscopes so that both the hair contaminant and a reference hair can be viewed at the same time. This procedure is similar to the way ballistics experts compare the markings on two bullets. With a comparison microscope, a determination can be made whether a hair came from a rat, a mouse, a human being, or any of a wide range of domestic and wild animals. Each FDA laboratory has a permanent collection of reference specimens from rats, mice, household pets, farm animals, local wildlife and exotic animals from foreign countries that frequently export food to the United States. A comprehensive collection will also include examples of other hair-like objects such as fibers from packaging materials, textile fibers, feather fragments, insect hairs and small worms.

The importance of accurately identifying hair contaminants found in food samples is twofold. First, the animal's identity is needed to evaluate the seriousness of the contamination. The action FDA takes regarding a defiled food may be governed to some extent by this information. Second, by identifying the source of the contamination, FDA officials can help the food handler to understand the causes of the problem so that effective steps may be taken to solve it.

Since the presence of rat or mouse hairs in food is often the first warning signal that rodents have invaded a food handling facility, FDA investigators may then conduct on-site inspections and collect additional samples of food or other evidence to show the extent of rodent activity present. This information must demonstrate the kind and approximate number of rodents involved, when and where rodent contamination of food occurred, how rodents gained access to the food products, and who was responsible for the unsanitary conditions that allowed rodents to defile the food.

A number of legal remedies are available to FDA for the protection of consumers from rodent-contaminated foods. Among these are seizure of contaminated goods, injunction against further manufacture or shipment of the products, and civil or criminal prosecution. Ultimately, the evidence developed by the FDA microscopist and investigators may be tested in a court of law to establish proof that a violation of the Food, Drug, and Cosmetic Act has occurred.

Information such as inspection findings and the results of the microscopist's examination of hair contaminants is also available to the food handler whose facility is afflicted with the rodent infestation. In many cases, this knowledge will be used by a firm to correct the rodent problem.

On a larger scale, the efforts of FDA to detect and identify evidence of rodent activity, such as hair contaminants, are an integral part of the intricate web of public services that protects Americans from the hazards of an unchecked explosion of rodent populations. To suppress the health menace of rats and mice, it is necessary for local, state and federal public health agencies to work together in a cooperative network of protection at all levels.

Alan R. Olsen is an entomologist in FDA's Los Angeles district laboratory.

On Narrowing The Patient-Doctor Communications Gap

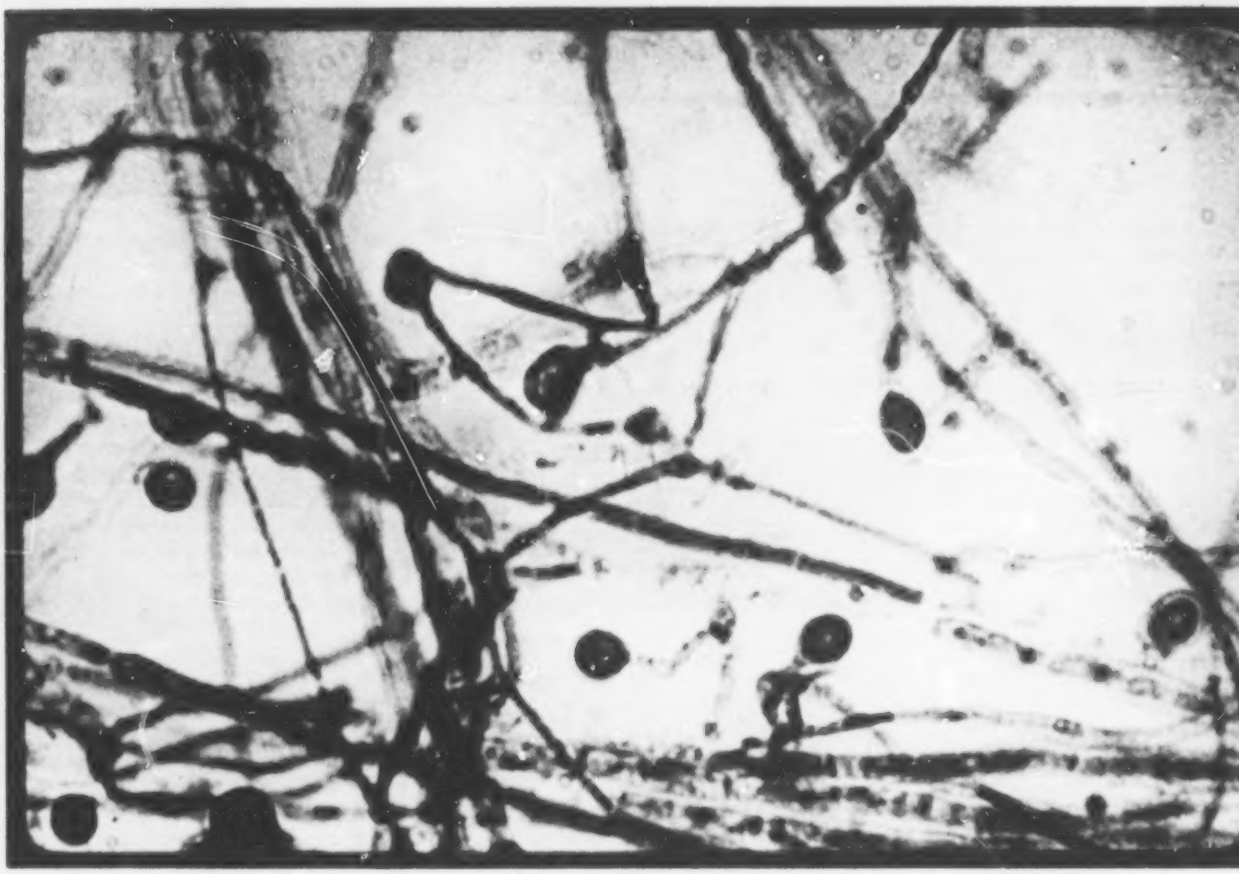
A good patient isn't always patient. In fact, sometimes impatience is rewarded. Take prescription drugs, for example. The good patient doesn't simply take his medicine without question. No, the good patient exercises his responsibility and his right. If instructions aren't forthcoming from the doctor or pharmacist, the patient asks how and when the medicine should be taken and what side effects it might cause.

Until recently, asking such questions was usually considered about as impertinent as inquiring of the Rolling Stones if they could follow a beat. But times are changing, and now health professionals are encouraging their members to answer a patient's questions before they're asked.

Much of this has come about because of a bit of bureaucratic meddling. Some might even say it was because of an attempt to over-regulate. That attempt was a proposal by the Food and Drug Administration to require patient package inserts (PPIs) for drugs. The PPIs would have been information leaflets to be handed out with prescriptions as they were filled.

The idea had advanced to the point where, in 1980, the FDA identified 10 classes of drugs that would be tested with PPIs in a three-year pilot program. That

About The Fungus Among Us



A mold culture of *Blastomyces dermatitidis*, the fungus responsible for North American blastomycosis.

The summer of 1970 promised to be exciting for a group of archeology students from Queens College of the City University of New York. They came to California to join similar students from Chico State College in excavating Indian ruins of the Northern Maidu, a civilization that existed about 1400 A.D. The "dig" was located about nine miles northeast of Chico in the foothills of the Sierra range, a three-hour drive up from San Francisco. As they sifted through the dry and dusty soil in search of beads, bones and arrowheads, the students dug up something they weren't expecting. At least 61 of the 103 people on the project developed coccidioidomycosis—also known as Valley Fever.

Those who are romantically inclined might speculate that this was a case of archeologists' illness, like the curse of King Tut's tomb, this time passed on by the spirits of the ancient Indians who were angered at being disturbed. The truth is more prosaic. Valley Fever is caused by a fungus common in the soil of the southwestern United States.

Valley Fever is one of about a dozen fungal diseases known in medical parlance as systemic or deep mycoses. Mycosis comes from a Greek word meaning fungus. In these diseases the fungus usually invades the lungs first and may then spread to other i
ternal systems. This is why they are called systemic. The sk
mouth, eyes and feet are other places where infection gets i
start.

There are other fungal type diseases such as candidal infe
tions caused by a yeast-like organism and superficial skin inf
tions including athlete's foot and ringworm. Many of these i
fections can be treated by drugs, both prescription and over-t
counter medications.

Fungi that cause systemic mycoses are found in many sit
They exist in spore form in the soil, in undisturbed dust and lin
in compost piles, organic wastes, chicken houses and pigeon pe
The tiny spores—two to three microns in diameter—are als
found in the damp basements of homes, in the tropics, pol
regions and the upper atmosphere. One medical article reporte
that fungal spores were found in the cellulose used to soundpr
and fireproof a hospital.

Because of their lightness, fungal spores may be carried on
wind. A freak dust storm that blew through southern Californi
in 1977 carried the Valley Fever fungus as far north as San Fra
cisco, Salinas, Stockton and Sacramento. Fungal spores ca

survive in a dry stage for months and even years.

The fact that these fungi can cause disease in humans and in animals is accidental, for nature did not intend them to be pathogenic. They became so because of their remarkable ability to adapt and grow at body temperature and to overcome man's natural defense mechanisms.

Although most systemic mycoses were identified well before the turn of the century, their names are not on the tip of most people's tongues, doubtless because they are not considered major illnesses. In fact, in most states fungal diseases don't have to be reported to health authorities. These diseases are usually mild and often there are no symptoms at all. But some can become chronic and if they spread throughout the body they can be serious, even fatal. People already weakened by other diseases such as leukemia, diabetes, emphysema or tuberculosis or whose immunological defenses are down because of treatment with drugs such as anti-bacterials or corticosteroids are particularly vulnerable. Fungi that take advantage of such situations are called "opportunists."

The list of systemic mycoses is tongue twisting. Besides coccidioidomycosis, try rattling off these names: histoplasmosis, aspergillosis, cryptococcosis, sporotrichosis and North American blastomycosis.

Valley Fever (also called San Joaquin Fever) is confined to the New World, infecting people in the desert areas of California, New Mexico, Texas, Nevada and southern Utah and in Mexico and parts of South America. Persons of both sexes and all ages are susceptible, but it is seen most often in men 25 to 55 years of age.

The most common primary form develops after a person inhales spore-laden dust. Frequently there are no symptoms or they may resemble those of a mild respiratory infection—fever, cough, chest pains and sore throat.

In a few cases the disease may progress by spreading to bones, joints, skin, intestines or brain, taking a few weeks, months, or even years after the first infection. Symptoms of the progression include a continuous low-grade fever, severe loss of appetite, loss of weight and strength and central nervous system disturbances. About 60 percent of these progressive cases are fatal. For some reason dark-skinned people are particularly susceptible to the progressive form of Valley Fever.

The acute form of histoplasmosis is usually mild with symptoms very like those of an upper respiratory infection. It can spread from the lungs through the body via the bloodstream, may affect the liver, spleen and lymph glands and occasionally cause ulcers in the mouth and intestines. An uncommon but serious complication that can occur here is Addison's disease, a type of adrenal disease with a high mortality rate. One form of histoplasmosis can cause cavities in the lungs similar to those caused by tuberculosis.

Histoplasmosis occurs throughout the world. In this country it is more common in the middle west, Alabama, Arkansas, Kentucky and Tennessee. The most likely victims are the very young and the elderly, particularly elderly men. Spores of this fungus exist in soil contaminated by bat and bird dung, including that from chicken houses.

The fungus that causes aspergillosis is an "opportunist," doing its dirty work in lungs already weakened by bronchitis or tuberculosis or in patients whose immunological defenses are weakened. In rare cases this disease will spread to other parts of the body such as bone, brain and heart.

Aspergillosis, too, is a worldwide malady. Men are affected more often than women and those in contact with grains and dusts are at greatest risk. Reports in France dating back to the mid-1800s describe aspergillosis as an occupational illness of pigeon-feeders and wigmakers who then used grain in their work.

Cryptococcosis also has worldwide distribution. In the United States more victims live in the southeast, are adults aged 40 to 60 and are men more often than women. This fungus occurs in the droppings of pigeons, although the birds themselves do not appear ill. The first site of attack is the lungs. This primary infection is usually without symptoms, although there may be a cough, a small amount of sputum, a slight fever and weight loss. The fungus characteristically spreads to the meninges (the covering of the brain), causing meningitis, and occasionally to the kidneys, bone and skin. Before antibiotic treatment was available, few patients survived cryptococcal meningitis.

Sporotrichosis is more likely to infect farm laborers, florists and horticulturists, especially those handling barberry bushes. The fungus responsible for this disease exists in soil, peat moss, decaying vegetation and on thorns. The first sign of the disease usually is a small, movable nodule, or lump, under the skin of the fingers. This lump gradually enlarges and ulcerates. In a few days or weeks similar nodules appear on the hands and arms. There usually are no other symptoms. When inhaled, the fungus can cause pneumonia.

North American blastomycosis afflicts men aged 20 to 40, chiefly in the southeastern states and the Mississippi river valley. Just where the fungus resides in nature is not known, but when inhaled it lodges in the lungs. Primary pulmonary blastomycosis begins as a mild respiratory disease with cough and chest pain. Patients sometimes cough up blood. As the disease gets worse the symptoms include fever, night sweats and loss of appetite and weight. Should the disease spread, it is most likely to appear on the skin although the prostate, testes, bone and subcutaneous tissues also may be involved. If untreated, the disease is slowly and fatally progressive.

Other systemic mycoses occurring in the United States are rhinocerebral phycomycosis, a usually fatal infection of the nose, sinuses and eye socket; maduromycosis (madura foot or mycetoma), chromomycosis and petriellidosis, all fungal infections of the feet. An infection that often starts in decayed teeth, actinomycosis, and a closely related disease, nocardiosis, were once thought to be fungal infections but are now known to be caused by bacteria.

Candidal type infections are caused by a yeast-like fungus that behaves somewhat differently from disease-causing fungi. It can reside in otherwise healthy people without causing any problems but becomes an "opportunist" when the host's defenses are down. Candidal infections, called candidiasis, can involve many parts of the body.

The oral form, also known as thrush, occurs most often in infants and in older people who are already victims of debilitating conditions. Creamy white patches appear inside the mouth and on the tongue and when scraped off leave a red sore. Thrush may spread to the pharynx and esophagus.

Another common candidal infection is vaginitis frequently seen during pregnancy and in women who have diabetes mellitus. Itching, burning and a white or yellow discharge with inflammation of the vagina are the usual symptoms.

Candidal infections can occur under the arms, in the groin, under the breasts, on the face, arms and legs, between the toes and on the scalp. The skin around the fingernails and the nails themselves can be affected.

Candidiasis also can become a systemic infection causing endocarditis, an infection of the inner lining of the heart; septicemia, a disease of the blood; or meningitis.

Until recently the treatment of severe systemic fungal and candidal infections was frustrating to physicians and patients alike. There were effective drugs, but some worked only against one or two infections, and others caused severe side effects. The first anti-fungal drug, potassium iodide, has been used since 1903 for the treatment of sporotrichosis. Another early medication, hydroxystilbamadine isethionate, is still considered effective against blastomycosis.

An antibiotic, amphotericin B (trade name Fungizone), used since 1957, is effective against virtually all of the major systemic fungal infections but unfortunately has drawbacks. It must be given intravenously over long periods and patients must be watched closely. The drug can cause kidney problems, depress the bone marrow (birthplace of red blood cells) and has other unpleasant, even potentially dangerous, side effects, such as phlebitis (blood vessel inflammation). Physicians are warned that amphotericin B is to be used only in patients with potentially fatal fungal infections and that the life-saving benefits of the drug should be balanced against its side effects.

Miconazole (Monistat), another intravenous drug, is marketed for treating severe cases of Valley Fever, systemic candidiasis, cryptococcosis and paracoccidioidomycosis (an infection similar to blastomycosis but found only in South America). Miconazole also is used to treat chronic mucocutaneous candidiasis, an infection of the lips, mouth and esophagus. Again there can be unpleasant side effects with this drug, including phlebitis, itching, rash, nausea and vomiting.

Another anti-fungal agent, flucytosine (Ancobon), has one advantage over both of these drugs—it can be taken orally. However, it is effective against only two types of infection, those caused by susceptible strains of candida and cryptocococcus. Close monitoring of patients with kidney or liver problems is required. Side effects include nausea, vomiting, diarrhea, rash and anemia.

A new drug with no serious side effects can be used for severe cases of histoplasmosis, Valley Fever, systemic candidiasis, chromomycosis and paracoccidioidomycosis. Ketoconazole was approved by FDA in June 1981, becoming the second drug for systemic fungal infections that can be taken orally. It is marketed under the trade name Nizoral. Ketoconazole is a new chemical entity and represents a significant therapeutic breakthrough.

An earlier breakthrough in the treatment of fungal diseases came in 1978 when FDA approved natamycin, an antibiotic, for fungal keratitis, an eye infection. Natamycin (Pimaricin) is the first ophthalmic product in the United States for this condition, which affects about 300 persons a year. Truly an "orphan drug," natamycin came on the market through an initiative by FDA's Bureau of Drugs and its Ophthalmic Drugs Advisory Committee and the manufacturer, Alcon Laboratories, Fort Worth, Texas. FDA compiled the data needed to show the drug was safe and effective and the manufacturer then agreed to formulate and market it.

At this point there is no protection against systemic mycoses except perhaps to stay out of areas where fungi reside. But, residents of Valley Fever areas may have something to look forward to. Scientists at the University of California's School of Public Health in Berkeley are working on a vaccine that may minimize the growth of the fungus in the lungs and prevent its spread to other organs. However, it may be three years at least before the vaccine is licensed.

The therapeutic picture for candidal skin infections is brighter. There are creams and ointments that can be applied directly to the affected areas with few or only mild side effects. These i clude amphotericin B cream (Fungizone Cream), miconazol nitrate (Micatin, Monistat), nystatin (Candex Lotion, Nilsta Mycostatin and others) and clotrimozole (Lotrimm, Gyne-Lotrimin). Mycotic vaginitis usually responds to these and t candicidin (Vanobid).

Far more common (and certainly easier to pronounce) are t so-called superficial fungal infections or ringworms, caused by fungi called dermatophytes.

There is ringworm of the body (tinea corporis) seen most oft in children. The infection consists of ring-like sores with a raised, red border of small pus-filled eruptions and a relative smooth central area.

Ringworm of the foot (tinea pedis) may be associated wi athletics because of its popular name, athlete's foot, but this condition is not exclusive to locker rooms. It is the most comm of the fungal infections affecting both men and women, although it usually occurs in males between the ages of 14 and It has been said that athlete's foot is the penalty man pays fo wearing shoes. The infection begins in the spaces between the t and may later involve the under surface of the arch of the foo Acute flare-ups are common during warm weather.

The nails of both hands and feet also can become the site o ringworm infection called tinea unguium. Toenail infection oft occurs along with athlete's foot; infections of fingernails are les common.

Ringworm of the scalp (tinea capitis) is another childhood in fection. It is usually spread from person to person and may become epidemic. Patchy bald spots, scaling and broken hair are common signs. The infection may be limited to a small are or spread over the entire scalp.

Fungal infections of the groin area, commonly called "jo itch," are common in men in the 18- to 40-year age group. Obesity, heat, sweating and tight clothing make it easier for t fungus to get its start in this condition, known medically as tinea cruris.

Fungi infections also may develop in the beard area and ar called, not surprisingly, tinea barbae. A superficial form loo like ringworm of the body. An acute form, contracted from animals, produces an inflammatory reaction with dischargin abscesses.

For those who suffer from these ringworm infections there a number of effective drugs on the market. Griseofulvin (trad names Fulvicin, Grifulvin, Grisactin) is effective and can be tak orally. Drugs that can be applied directly on the infected area include haloprogin (Halotex), miconazole nitrate and clotrimazole.

Some over-the-counter or non-prescription drugs also can used to treat some of these superficial fungal infections. A pane of experts reviewing the safety and effectiveness of preparatio for athlete's foot, jock itch and ringworm of the skin said thes ingredients will do the trick: iodochlorhydroxyquin, tolnafta and undecylenic acid and its salts (calcium undecylenate, coppe undecylenate and zinc undecylenate). The panel also recomme ded three ingredients now available by prescription only: haloprogin, miconazole nitrate and nystatin. To be labeled the treatment of athlete's foot, jock itch and ringworm, nystati must be used in combination with other anti-fungal agents, t panel said. The report of this panel, one of 17 advisory grou assisting in FDA's review of all over-the-counter drugs, was published for public comment in the March 23, 1982, *Feder Register*.

— Annabel Hec

The Notebook

The Notebook: a potpourri of items of interest to consumers, gathered from FDA press releases, other news sources and the Federal Register *(designated FR with date of publication). The* Federal Register *is available in many large public libraries.*

■ Dr. Lester Crawford, DVM, Ph.D., has returned to the post of director of **FDA's Bureau of Veterinary Medicine,** a position he held from August 1978 to August 1980. In the interim, Dr. Crawford was head of the Department of Physiology-Pharmacology at the College of Veterinary Medicine, University of Georgia.

■ U.S. drug industry exports rose 16.8 percent in 1981 to $2.3 billion and imports grew 6.7 percent to $965 million over the previous year, according to a Commerce Department report **"1982 U.S. Industrial Outlook."** Biologicals grew the fastest, with shipments increasing 35 percent to $523 million. Exports of active ingredients ("medicinals and botanicals") came to $1.3 billion, while exports of pharmaceutical finished products—both OTC and prescription drugs—rose to $490 million in 1981, according to the Commerce report. The department also predicts that vitamin sales in the United States will nearly triple between 1980 and 1988, reaching $3.5 billion by that year. The Commerce Department report is available from the Superintendant of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

■ If FDA lowers its **tolerance for PCBs** in fish and shellfish to two parts per million (ppm), as the agency proposed in 1979, $86.7 million worth of food would be lost each year, according to Administrative Law Judge Daniel J. Davidson. The National Fisheries Institute (NFI) and others had objected to the 1979 proposal because they felt the decision was based on faulty estimates of loss. FDA had estimated that food losses would be $5.7 million in 1974 dollars compared to a loss of less than $1 million at the present tolerance of five ppm. These estimates were dockside values. NFI argued that the real loss when the fish were cleaned, canned, distributed and sold at retail would be over $500 million.

The loss in value, figured in 1980 dollars, will be one of several factors in FDA's final decision whether to lower the PCBs tolerance or keep it at five ppm.

■ The major active psychotropic substance in **marijuana,** tetrahydrocannabinol (THC), should not be put in a less restrictive controlled drug category until, and if, it is approved for use in cancer chemotherapy. That's the recommendation of FDA. A New Drug Application is pending before FDA on THC seeking approval to market the product for treatment of nausea and vomiting in patients undergoing cancer chemotherapy. At present, THC is in Schedule I of the Controlled Substances Act. That is the most restrictive schedule. FDA says if it is approved for therapy it should move to Schedule II (FR Mar. 9).

■ To keep duplication of inspectional efforts to a minimum, FDA and the Food Safety and Inspection Service, USDA, have entered into an agreement to provide each other with **information on violations** by food manufacturers whose facilities are under both FDA and FSIS jurisdiction. The agreement became effective in June 1981 (FR Feb. 19).

■ Under an agreement, effective Jan. 12, 1982, the **Centers for Disease Control** will alert FDA whenever there is an epidemic possibly associated with the use of agency-regulated products. CDC will also supply lab data when information on safety and effectiveness of such products turns up in its investigations. FDA, in turn, will alert CDC to product-associated infections and disease outbreaks encountered during its investigations (FR Feb. 19).

■ The Consumer Product Safety Commission has made final the exemption from the **child-protection packaging requirements** of all unit-dose forms of potassium supplements containing not more than 50 milliequivalents of potassium per unit dose. The commission is proposing to exempt from these requirements prednisone in tablet form in packages containing no more than 105 milligrams of the drug (FR Mar. 10).

■ FROM THE MARKET BASKET: **Locust bean gum** is not a carcinogen (cancer-causing agent), at least where rats and mice are concerned, according to a study carried out by the HHS National Toxicology Program. The gum is used as a food stabilizer in ice cream, sauces, salad dressings, pie fillings, jams and jellies, as a binder in processed meats, and in the manufacture of drugs, cosmetics, textiles, paper, ceramics, paint and gun powder (FR Feb. 24). . . . Some meats will be cured faster, thanks to a rule finalized by the USDA permitting the use of **fumaric acid** as a cure accelerator in cured, comminuted (ground up) meat and poultry products. An FDA-approved food additive, fumaric acid accelerates color fixing, allows use of higher cooking temperatures and shorter preparation time (FR Feb. 22). . . . Because of a petition by the Malaysian Pineapple Industry Board and other objections, FDA has put a halt to its **new standard of identity** establishing new designations for different styles of pineapple (FR Mar. 9).

Investigators' Reports

Lies Add Up To A Year In Prison

by Carol Ballentine

It was an intricate pattern of lies that Dr. James J. Scheiner wove. It took a grand jury investigation and some lengthy detective work by FDA's Baltimore district to unravel the doctor's deceptions, practiced on FDA and several major drug companies.

Scheiner's basic deception involved fictitious reports about clinical investigations of three drugs, investigations he had agreed to perform for their manufacturers. Scheiner, an orthopedic surgeon practicing in Virginia, had agreed to test the drugs on his patients to prove their safety and effectiveness. He had accepted money from the manufacturers for the work and submitted clinical data on the drugs to the companies to be filed with FDA to support New Drug Applications.

FDA began to suspect the doctor was not conducting his drug studies in an approved fashion during a routine inspection by the Baltimore district. The district wrote Scheiner, advising him that two investigators would, within two weeks, come to inspect the records concerning the drug studies. The advance notice was a courtesy to allow him to reschedule patient appointments. When the investigators got to Scheiner's office, he told them the office had been broken into three times since the FDA notification letter had been received. During the first break-in, the doctor said, vandals had thrown most of the pertinent drug study records into a whirlpool bath; they were so water soaked, he said, he had had to throw them away. In the second break-in, he told them, a fire had started mysteriously in the X-ray room, destroying other documents. During a third break-in, Scheiner said, he had been attacked, struck in the head with a piece of pipe, and suffered a laceration of the scalp and cerebral concussion.

The investigators checked the story with the police department, which expressed skepticism that the break-ins had occurred. For one thing, their investigation indicated that Scheiner had been the last person seen to leave the X-ray room before the fire, and it started about six minutes after he left. Further, police analysis of the piece of steel identified as the weapon used to attack the doctor revealed only one palm print—Scheiner's.

When the investigators began comparing the remaining patient records against the clinical reports sent to the drug companies, they found serious discrepancies—differences in patients' ages, sexes, diagnoses and the medications they were taking (which could have skewed the test results). Most of the patients contacted for statements denied they had participated in any drug studies.

The agency's Bureau of Drugs wrote Scheiner, asking for an informal conference to explain the various discrepancies. He replied that he couldn't because the records had been destroyed during the break-ins.

Summoned to a hearing by the Baltimore district, Scheiner brought along his attorney and a former employee, Earl R. Walker, who stated that he had been involved in the drug studies and had helped extract information from them. But Scheiner still was unable to explain the discrepancies to FDA's satisfaction, and the Bureau of Drugs subsequently notified him that he was no longer entitled to receive investigational drugs or act as a clinical investigator.

FDA then initiated a grand jury investigation, which involved months of gathering evidence and interviewing witnesses. Scheiner was indicted on 19 counts, including charges of mail and wire fraud and of submitting false documents to the federal government. He pleaded not guilty.

Part of his defense rested on a letter written by Earl Walker, his former medical assistant. Scheiner's attorneys told the court that the doctor had received the letter in which Walker admitted responsibility for the conduct of the suspect drug studies. The defense attorneys insisted that Walker was a material witness who could provide evidence to this effect. The problem was that Walker could not be found, even though he had been under subpoena to appear before the grand jury.

Suddenly the district received a call from Walker. He was at his parents' home in Kentucky. Several investigators interviewed him in the presence of a U.S. marshal, who held a second subpoena charging him with failing to obey the first subpoena.

Walker told them that after he had received the grand jury subpoena he had called Scheiner, who insisted he fly to Washington, D.C., at Scheiner's expense. From the airport Walker was taken to a hotel in Fairfax, Va., he said, where Scheiner gave him wine and drugs. It was here, Walker said, that Scheiner dictated the letter in which Walker assumed responsibility for the drug studies, a letter Walker copied and then signed. Walker said that Scheiner told him he did not have to obey the grand jury summons. Over the next few weeks, while the grand jury investigation was going on, Walker said that Scheiner transported him to a number of motels and hotels in Virginia and North Carolina, paying all the bills and supplying alcohol and drugs. Walker told the investigators that most of the time he was drunk and drugged and finally passed out in a motel room. The motel manager called the rescue squad and Walker was taken to a hospital and eventually to his parents' home in Kentucky. It was then that he called FDA.

Walker's story was substantiated by the district, which then presented it to Scheiner's attorneys. Scheiner admitted the story was true and agreed to plead guilty to three counts of submitting false statements to FDA, in exchange for which the agency agreed not to bring any indictments for obstruction of justice.

On Dec. 11, 1981, after an appeal by Scheiner's attorney urging that the court permit Scheiner to perform community service in lieu of being sentenced, Judge William Bryant of the U.S. District Court for the Eastern District of Virginia sentenced Scheiner to seven years' imprisonment, six years of which were to be suspended. Scheiner was then sent to federal prison for one year and will be on supervised probation for three years afterward. He was fined $30,000.

Carol Ballentine is a member of FDA's Public Affairs staff.

Swift Justice

There was no welcome mat out for a shipment of shucked oysters that arrived last December in Baltimore from Virginia.

Maryland health authorities had been alerted that these oysters were "uncertified," meaning that they were taken from Virginia waters closed to oystering because of contamination.

The **Virginia Bureau of Shellfish Sanitation** had called the Maryland authorities at 10 a.m. one day that month, as the oysters were being unloaded in Baltimore. The Maryland officials moved quickly and embargoed the entire lot, which prevented its being sold. They then delivered a sample of the oysters within an hour to a Virginia investigator waiting at the Maryland-Virginia state line.

The investigator moved just as quickly, getting the sample half an hour later to the Westmoreland, Virginia, county courthouse, where the firm that had done the shipping was to go on trial.

Faced with the just-delivered evidence, which they had not expected to see, the company's officers decided to settle out of court. The firm accepted an injunction prepared by the Virginia state's attorney restricting further shipments of oysters by the company, and those oysters already held or shipped by the firm were destroyed, including the ones in Baltimore that had provided the evidence.

Door-to-Door No More

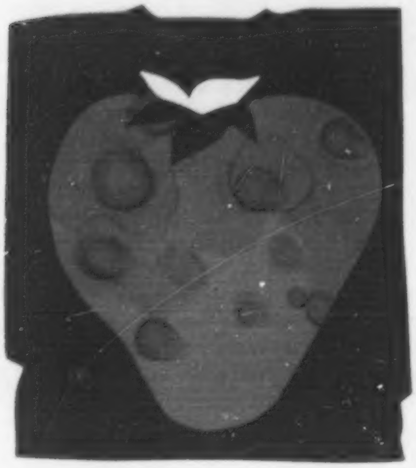
Two children in Albany, N.Y., noticed some interesting looking packages on the front steps of several houses in their neighborhood. They went from door to door picking up the packages and finally managed to open one despite its child-resistant lid. About this time they wandered into a small local grocery store and the curious owner asked what they had. "Candy," said the children.

But it wasn't. It was Comtrex, a nonprescription cold medication being distributed door-to-door by an advertising firm. Each sample package held eight yellow Comtrex tablets, and together these contained enough of an aspirin substitute called acetaminophen to be potentially toxic for a small child. For a 2-year-old, three grams of acetaminophen—the amount in about nine tablets of Comtrex—can cause liver damage. Larger overdoses of acetaminophen can be fatal. Comtrex also contains a decongestant, antihistamine and cough reliever.

Fortunately, the store owner grabbed the packages from the children (ages 3 and 4) before they could swallow any tablets. She then complained to a local newspaper, and the resulting publicity led to an investigation by FDA's **Albany resident post** as well as local police and consumer protection agencies.

FDA collected samples and learned from the local agencies that Audited Advertising Distributors Inc., of Great Neck, N.Y., was distributing Comtrex for the manufacturer, Bristol-Myers. Since Albany is located in FDA's **Buffalo district,** the Buffalo district director called Bristol-Myers and voiced FDA's objections to door-to-door distribution of non-prescription medicines. The chief concern was that children could easily find them and take potentially harmful doses.

Shortly afterward, Bristol-Myers informed FDA that it had halted all door-to-door distribution of Comtrex.



Growth Product

Discovery of mold on food—or on clothes, walls, bathroom fixtures and other surfaces that the stuff likes to adhere to—can cause dismay and indignation. If it's on food, drugs or cosmetics, mold can also generate action by FDA.

The agency's **Seattle district** encountered this age-old contaminant during a routine inspection of Valley Packers, a company that processes frozen strawberries in Puyallup, Wash. Samples collected during the inspection contained excessive mold. At the district's request, 306 28-pound cans of strawberries, valued at $5,500 retail, were seized by the U.S. marshal for Seattle.

Similarly, the **Detroit district** moved after receiving two consumer complaints about black particles in Massengill twin-pack water-vinegar disposable douche kits. An investigator collected a sample, and the solution in the kit was found to contain 33,000 mold organisms per milliliter—excessive by FDA standards.

The distributor of the kits was a Detroit company. However, the product's manufacturer, Beecham Products, was located in Clifton, N.J., so the district notified its counterpart in Newark. A subsequent inspection by a **Newark district** investigator indicated that the contamination could have been caused by a piece of defective filtration equipment—a problem the firm easily corrected.

The visible mold particles were found only in one lot of the douche solution, and samples collected from other batches were found free of contamination. However, the Detroit distributor initiated a recall of all lots that might have been contaminated due to the defective equipment. The recall is being monitored by the Detroit district.

PCBs Fallout

The main transformer that handles electrical power for buildings in the restored Quincy, Mass., Waterfront Market exploded in mid-January, sending smoke and fumes throughout the complex and forcing a noontime crowd of 2,000 people to head for the exits.

There was no real fire and damage to the building was minimal. But the sealed transformer held 100 gallons of an oily liquid that contained a toxic chemical, polychlorinated biphenyls (PCBs). This had spilled onto the floor of the transformer vault in the basement, and fumes from the PCBs had been carried through the three market buildings by the ventilation system. Four persons were treated for fume inhalation at a nearby hospital and released.

The Market is a Boston showplace, a restored former warehouse area that centers around historic Faneuil Hall, where the Boston Tea Party of the American Revolution was planned.

Hardly had the firemen left when state food and drug and Boston health department officials were going through the buildings and concourse areas that house 170 retail stores, many of them food specialty and restaurant operations. They were aided by two FDA investigators, who came over from FDA's **Boston district** office a few blocks away. The officials needed to be certain that neither the fumes nor the liquid PCBs, although the latter were confined to the basement, had contaminated any food products. FDA's Boston laboratory assisted by running tests on samples from exposed and packaged foods and serving and storage areas.

No PCBs contamination was found, except in the vault area itself. However, the entire complex was closed for two days to allow for a thorough cleanup, and health officials continued checking through the buildings for a month for possible residual effects.

PCBs are industrial chemicals once widely used as solvents and stabilizers in paints, plastics, pesticides and other products. In the early 1970s it was realized that PCBs are highly toxic to human and animal life, especially to the central nervous system. Their indestructability had been a virtue in certain types of chemical processing, but when it was found that they were toxic, this characteristic became an added danger. Once in the environment or the food chain, PCBs are persistent. They will not break down into harmless substances. That is why a PCBs spill is so alarming.

PCBs have fewer uses now, but they are still permitted in sealed electrical transformers as a liquid, non-flammable coolant and insulation. Transformer leaks and explosions will predictably release PCBs, and emergency action must be taken.

A Week in the Life of . . .

Day 1. Inspector from FDA's **Los Angeles district** office picks up samples of assorted produce on a routine survey trip through growing areas west of the city.

Day 2. Inspector drops off samples at district laboratory, where they will be tested for pesticide residues. Later in the day, laboratory reports that spinach tests high in residues of Monitor, a pesticide illegal for that crop. Notes show sample came from Pleasant Valley Vegetable Cooperative, a marketing co-op at Oxnard, 60 miles from Los Angeles.

Day 3. Investigator checks with Pleasant Valley, learns that spinach in question had been shipped two days earlier (coincidentally, the day the sample was taken) to a wholesaler in Chicago. Investigator gets detailed shipping information and alerts FDA's **Chicago district** office so that it can locate the spinach and get an end-point (delivered) sample for analysis.

Day 4. Chicago investigators find entire shipment (119 cartons, 24 pounds to a carton) of Pleasant Valley spinach at the South Water Street Market, where it arrived the day before. Investigators arrange for lot to be held there, to prevent its being sold, then send a sample by air to FDA's Minneapolis laboratory for a confirmation analysis, testing for the pesticide. Back in Los Angeles, investigators visit the Oxnard growing fields to determine how Monitor got on the spinach. Growers deny ever using the pesticide.

Day 5. Chicago district asks FDA Washington headquarters (Bureau of Foods) to authorize seizure of the spinach. Bureau compliance officers give tentative approval, pending the Minneapolis laboratory report. Minneapolis calls Chicago to say that the end-point samples were positive for Monitor.

Day 6. With Monitor found in both shipping (Oxnard) and delivered (Chicago) samples, bureau officials approve the seizure.

Day 7. FDA Chicago district obtains a court order directing seizure of the contaminated spinach. Investigators return to South Water Street Market, where a U.S. marshal carries out the court order. Spinach is trucked to a landfill and destroyed by burial.

Mixed-Up Drug

Philips Roxane is a pharmaceutical manufacturing firm in Columbus, Ohio, that supplies drugs to hospitals and health care facilities, to be given under medical supervision. The firm's entry in the *Physicians' Desk Reference*, a descriptive drug listing for the medical profession, stresses that "each hospital dose unit of Roxane medication moves from the production line to the patient's bedside in tamper-proof containers, labeled for positive identification and protecting dosage integrity to the point of administration."

Despite Roxane's precautions, a 10-ml container of chloral hydrate, a hypnotic drug and sedative, turned up in a Reidsville, N.C., hospital labeled as diphenhydramine hydrochloride elixir, an antihistamine syrup. The containers resemble the little single-service cups of coffee cream with sealed foil tops. The label for the medication is printed on the foil.

The hospital pharmacist at Reidsville reported the error to FDA's Raleigh resident post. The agency's **Cincinnati district** office was asked to investigate, since Roxane is located in that district.

Checking the company warehouse showed that all its chloral hydrate syrup was properly labeled. Checking the label storage area and the packaging and labeling operation showed nothing wrong. This appeared to be a one-container error, already caught. Roxane saw no reason to recall the medication.

Then a month later Roxane received a second complaint, this time from a hospital in Pennsylvania, saying that three containers of chloral hydrate were mislabeled as antihistamine. The containers had the same lot number as the earlier mislabeled container. With this second finding, Roxane agreed to recall all chloral hydrate with that lot number, not difficult to do since the product had gone only to hospitals and not to the public.

A few additional errors were found in the products returned, but there was no way to reconstruct how the mislabeling had occurred. No injuries or harmful effects were reported from the mixup.

Problem Cannery

More than 20,000 cases of various meat and vegetable products were destroyed and a massive recall instituted after an FDA investigator discovered serious processing deficiencies at a Los Angeles cannery. For the owner, the Church of Jesus Christ of Latter Day Saints (LDS), the cost of the destruction and recall effort was estimated at more than $1 million.

During a routine inspection of the cannery, a **Los Angeles district** FDA investigator found extensive evidence of shortcutting or elimination of important processing steps and practically no quality control. Since the cannery dealt with low-acid foods, processing deficiencies increased the risk that *Clostridium botulinum* spores could survive and produce deadly toxin in the canned products.

A number of sample cans were collected and analyzed by the Los Angeles district laboratory. Although no bacterial growth or gas was confirmed, many cans displayed physical characteristics normally associated with improper processing such as swollen lids that could be pressed down. Also, some cans of the same product varied appreciably from one to another in fill of solids and liquids. This could result in underprocessing of cans containing denser materials since they would need longer cooking times.

The investigator also discovered numerous errors and misstatements among the processing records. In 34 instances, recording thermometer charts had been filled out partially or totally by hand (the charts are normally produced automatically by machine). Many of the cannery operations were performed by inadequately trained volunteers, although records indicated they had been done by two professionals hired by the cannery.

Since some products being processed included some or all meat, and thus come under jurisdiction of the U.S. Department of Agriculture, USDA was informed of the situation. USDA and the State of California each sent officials to the cannery, then authorized FDA to act on their behalf during the remainder of the four-week inspection.

After learning of FDA's findings, LDS officials ordered a recall of products produced by the cannery in the past three years. Since the canned goods had been distributed free to church members in California, Nevada, Utah and Hawaii, the recall meant that thousands of people in those states had to be contacted personally. In addition, the church agreed to destruction of more than 20,000 cases of canned goods and closed down the cannery.

—Compiled and written by Carol Ballentine, Louise Fenner and Richard Thompson.

Postal Service Cases

U.S. POSTAL SERVICE

actions taken in medical cases as authorized in the Mail Fraud Statute (18 U.S.C.
False Representation Statute (39 U.S.C. 3005) as reported by the Chief Postal Inspecto

False Representation Orders Issued by Judicial Officer Under 39 U.S.C. 3005

November 30, 1981: Against **Slim Quick,** Box 893, Metuchen, N.J. Satisfactory evidence was presented to the Postal Service that Slim Quick and its agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Slim Quick." The ad states, in part, "lose up to 12 pounds in 7 days! Up to 20 pounds in 14 days! You can lose those embarrassing extra pounds quickly and safely!"

November 30, 1981: Against **Doctor's Capsule Plan,** Box 398, Bronxville, N.Y. Satisfactory evidence was presented to the Postal Service that Doctor's Capsule Plan and its representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Doctor's Capsule Plan—Diet Capsule," representing the ability to "melt away fat forever."

November 30, 1981: Against **G.H.P. Laboratories,** 1551 Dunwoody Village Pkwy., P.O. Box 888651, Atlanta, Ga. Satisfactory evidence was presented to the Postal Service that G.H.P. Laboratories and its representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Gerovital HP Capsules and Cream." The ad states, in part, "Gerovital HP can help keep you young . . . completely natural, totally safe and guaranteed to provide satisfactory results . . . Gerovital HP Cream for soft, moist, more youthful skin . . . to nu
healthy new skin. Your skin will look and feel youn
it has in years."

December 11, 1981: Against **La Fleur Natural,** P.O. Box 1
Satisfactory evidence was presented to the Postal Se
Natural and its agents are engaged in conducting a s
obtain money by means of false representation. The
ing the product "Brainpower." The ad states, in pa
mind to its fullest. These herbs, along with others, ma
new Brainpower formulation. If you're interested i
extending the capabilities of your mind, be sure to
power today."

December 11, 1981: Against **Earthquest Ltd.,** P.O. Box 4
Satisfactory evidence was presented to the Postal S
quest Ltd. and its representatives are engaged in co
or device to obtain money by means of false repres
was advertising the product "RNA-Tablets and Cre
the ability to "prolong your youthful, beautiful appe
ing and smoothing your face with RNA Cream. You
supple, diminishing crow's feet and wrinkles."

Complaints Filed by Law Department Under 39 U.S.C. 3005 (False Representation)

November 3, 1981: **Renee Renoir,** 1626 N. Wilcox, Hollywood, Calif. Advertising and sale through the mail of the product "Le Grand Big Bosom Creme and Big Bosom Le Grand Pills," representing the ability to "enlarge your bosom . . . increase your bustline up to 6 inches and 3 cup sizes!"

November 3, 1981: **Lawrence Larrabee,** 663 Fifth Ave., New York, N.Y. Advertising and sale through the mail of the product "Aero-Plus 3." The ad states, in part, "enlarge your bosom 3 full cup sizes in only 7 days!"

November 3, 1981: **Jules J. Garfield,** 1626 N. Wilcox, Suite 366, Hollywood, Calif. Advertising and sale through the mail of the product "Placenta Big Bosom Creme with Magnum Cup Expander." The published advertisement states, in part, "The A, B, C (and D's) of Breast Enlargement . . . increase your bust up to 6 inches and 3 cup sizes."

November 3, 1981: **Frederick French,** 30 Montrose Ave., New Brooklyn, N.Y. Advertising and sale through the mail of the product "Living Fluid and Living Creme," representing the ability to "enlarge your bosom . . . be big busted beautiful in an era of small bosomed women . . . gain up to 6 inches and 3 cup sizes now!"

November 3, 1981: **R. Scott Fitzgerald,** P.O. Box 2700, Ne
vertising and sale through the mail of the produc
Bosom Creme and Big Bosom Le Grand Pills." The
"enlarge your bosom . . . increase your bustline up to
sizes!"

November 3, 1981: **Dimensions,** P.O. Box 35276, Los Ang
tising and sale through the mail of the product "Di
Enlarger." The ad states, in part, "Dimension Pl
penis 2 to 3 inches longer, also thicker and firmer. I
trol premature ejaculation."

November 4, 1981: **Charles C. Cunard,** 210 Fifth Ave., Ne
vertising and sale through the mail of the product "P
Creme & Magnum Cup Expander," representi
"produce gains of six inches and three cup sizes in
breast in only ten days . . . will cause the female user
to six inches . . . ."

Notices of Judgment

NOTICES OF JUDGMENT on Seizure Actions

FOOD / Poisonous and Deleterious Substances

Salmon eggs (several commingled lots), at Duluth, Dist. Mich.

Charged 12-15-77: when shipped by Toots Market, Algoma, Wis., and/or Bell Fisheries, Mackinaw City, Mich., the article contained the added poisonous and deleterious substance polychlorinated biphenyls, and the quantity of polychlorinated biphenyls in the article exceeded the prescribed 5 ppm tolerance; 402(a)(2)(A). Consent decree authorized release to A. Kemp Fisheries Inc., Duluth, Minn., for salvaging. (F.D.C. No. 61458; S. No. 78-129-103; N.J. No. 1)

Swordfish steaks, at Rochester, W. Dist. N.Y.

Charged 9-15-80: when shipped by Palmer Fish Co. Inc., Rochester, N.Y., the article contained the added poisonous and deleterious substance mercury in a quantity which might render it injurious to health; 402(a)(1). Default decree ordered destruction. (F.D.C. No. 63175; S. No. 80-174-619; N.J. No. 2)

FOOD / Contamination, Spoilage, Insanitary Handling

Fructose, at Cleburne, N. Dist. Texas.

Charged 6-9-81: while held by Keene Distributors, Cleburne, Texas, the article had been held under insanitary conditions; 402(a)(4). Default decree ordered destruction. (F.D.C. No. 63482; S. No. 81-265-623; N.J. No. 3)

Halibut, dressed & headed, frozen, at Mount Vernon, W. Dist. Wash.

Charged 9-11-81: when shipped by Sitka Sound Seafoods, Sitka, Alaska, the article contained decomposed fish; 402(a)(3). Consent decree authorized release to Todd Savage, Seattle, Wash., for salvaging. (F.D.C. No. 63532; S. No. 81-277-859; N.J. No. 4)

Rice, bulgur wheat, spices, mung beans, and **other foodstocks,** at Boston, Dist. Mass.

Charged 3-28-79 and amended 5-4-79: while held by Mayco Packing & Storage Co.Inc.,Boston, Mass. , all of the articles had been held under insanitary conditions—402(a)(4); some of the articles contained rodent filth—402(a)(3); and the mung beans contained insect filth and contained the nonconforming pesticide chemical endrin—402(a)(3), 402(a)(2)(B).

The mung beans were claimed by Wallant International Trade Inc., New York, N.Y. The rice, wheat, spices and other foodstocks were claimed by Syrian Grocery Importing Co. Inc., Boston, Mass. Mayco Packing & Storage Co. Inc., Boston, Mass., also filed a claim to the articles as an interested third party. Pursuant to stipulation of the parties, Mayco Packing & Storage Co. Inc. consented that an order be entered prohibiting it from storing food at its warehouse. Post-seizure sampling of the mung beans by Wallant International Trade Inc., for testing for endrin, for insect and rodent filth, and for ability to sprout was authorized.

A consent decree authorized release of the articles claimed by Syrian Grocery Importing Co. Inc. to that claimant for salvaging. Subsequently, a consent decree of condemnation authorized release of the mung beans to Wallant International Trade Inc. for salvaging. An amended consent decree authorized additional time for reconditioning the mung beans, a corrected bond amount, and a reconditioning plan. (F.D.C. No. 62187; S. No. 79-160-527; N.J. No. 5)

Shrimp, broken, canned, at Dulac, E. Dist. La.

Charged 4-7-81: when shipped by Calvin J. Authement Packing Co., Dulac, La., to Vancouver, Canada, refused entry, and reshipped to New Orleans, La., the article, labeled in part "Four Star . . . Broken Shrimp . . . Product of U.S.A. . . . Prepared For . . . Shafer Haggart Ltd. Vancouver, Canada," contained decomposed shrimp; 402(a)(3). Consent decree authorized release to the packing company for salvaging. (F.D.C. No. 63427; Import S. No. 282073; N.J. No. 6)

Walnuts, at St. Paul, Dist. Minn.

Charged 10-20-81 and amended 10-26-81: while held for sale, the article contained insect filth and moldy decomposed walnuts; 402(a)(3). Default decree ordered destruction. (F.D.C. No. 63576; S. No. 81-218-632; N.J. No. 7)

FOOD / Economic and Labeling Violations

"Maple Syrup," at San Antonio, W. Dist. Texas.

Charged 1-16-81: when shipped by Howard Fortenberry, Philadelphia, Miss., the article had had corn syrup substituted for maple syrup—402(b)(2); the article's labeling was false and misleading because it represented that the food consisted wholly of maple syrup—403(a)(1); and the article failed to conform to the definition and standard of identity for maple syrup, since the article was made with syrup derived from a source other than the maple tree—403(g)(1). Consent decree ordered destruction. (F.D.C. No. 63272; S. No. 81-193-032; N.J. No. 8)

"Orange juice" for manufacturing, concentrated, at Worcester, Dist. Mass.

Charged 11-30-81: when shipped by Fresh Pak Foods, Weslaco, Texas, the article, labeled in part "Fresh Pak Foods, Inc., McAllen, Texas . . . Concentrated Orange Juice for Manufacturing," had had the color turmeric added to the article so as to make it appear better and of greater value than it was—402(b)(4); the article contained the non-conforming color additive turmeric, since there was no effective regulation permitting the addition of turmeric to concentrated orange juice for manufacturing—402(c); the article's labeling was false and misleading in claiming that the article was concentrated orange juice for manufacturing—403(a)(1); the article failed to conform to the definition and standard of identity for concentrated orange juice for manufacturing, because the article contained the added color turmeric—403(g)(1); and the article contained the artificial coloring turmeric and its label failed to state that fact—403(k). Default decree authorized donation to a charitable institution. (F.D.C. No. 63584; S. No. 81-255-681; N.J. No. 9)

"Sorghum" syrup in jars, cans, and buckets, at Perkins, W. Dist. Okla.

Charged 10-14-81: while held by Sooner Valley Honey, Perkins, Okla., the article, labeled in part (jars) "County Sorghum Made By Elmer Eakes Philadelphia, Mississippi," (cans) "Ole Fashion County Sorghum Made By Elmer Eakes . . . Philadelphia, Mississippi," and (buckets) unlabeled, had had glucose syrup substituted for sorghum—402(b)(2). The labels of the article in jars and cans bore false and misleading claims representing that the article consisted wholly of sorghum—403(a)(1); the article in jars and cans failed to conform to the definition and standard of identity for sorghum, since the article was made with syrup derived from a source other than sorghum cane—403(g)(1); the article in buckets lacked labels containing the name and place of business of the manufacturer, packer or distributor and lacked an accurate quantity of contents statement—403(e); the article in buckets lacked labels containing the common or usual name of the food—403(i); and the article in jars and cans was in violation of the Fair Packaging and Labeling Act, since the quantity of contents statements were not expressed in fluid ounces followed in parentheses by a declaration of the largest whole unit of net quantity of contents, and the quantity of contents statement on the article in jars, which had a principal display panel area of more than five square inches, was in a type size less than ⅛ inch high—15 U.S.C. 1453(a)(3)(A)(i), 1453(a)(3)(C)(i). Default decree condemned the articles and ordered them constructively destroyed by delivery to a charitable institution for use and not for resale. (F.D.C. No. 63566; S. No. 81-265-532; N.J. No. 10)

FOOD ADDITIVES

Nature's Herbs capsicum & lobelia combination desert herb capsules, and **Nature's Herbs dandelion, golden seal, yellow dock root & lobelia combination capsules,** at South San Francisco, N. Dist. Calif.

Charged 2-26-81: when shipped by Nature's Herbs Inc., Orem, Utah, the articles contained the non-conforming food additive *Lobelia inflata L.*—402(a)(2)(C). Default decree ordered destruction. (F.D.C. No. 63337; S. No. 81-239-414 et al.; N.J. No. 11)

L-tryptophan tablets, at Moonachie, Dist. N.J.

Charged 2-22-77: the article, which had been manufactured by Leeds-Dixon Laboratories Inc., Moonachie, N.J., using interstate tryptophan powder, was the non-conforming food additive L-tryptophan, since its use and intended use was not in conformity with a regulation or exemption—402(a)(2)(C).

The article was claimed by the dealer-manufacturer who denied the charge, asserted that the article was not a food additive, and asserted that the sale of the article was neither inconsistent with 21 C.F.R. §121.1002 nor with §121.101(d)(5). The claimant served several sets of written interrogatories on the government. The government served writ-
ten interrogatories and requests for admissions on t
claimant moved for summary judgment. The court gr
saying:

"This matter is before the court on claimant's mo
judgment pursuant to Fed.R.Civ.P. 56(c). Accor
evaluates the motion in light of the 'genuine issue of m
dard.

"The action arises out of the seizure by the United
pursuant to the authority of 21 U.S.C. § 334, of thre
follows: '2 DOZ. L-TRYPTOPHAN 30 * * *
NATURAL L-TRYPTOPHAN 3 Tablets = 2 gram
$8.00 Manufactured by SCHIFF BIO-FOOD PRO
dietary supplement, take 3 tablets after the evening m
time. Each tablet contains 667 mg. Three tablets sup
TRYPTOPHAN. L-tryptophan is an essential Ami

"The complaint alleges that the L-tryptophan
adulterated within the meaning of the Food, Drug, a
21 U.S.C. § 301 *et seq.*, since its use does not confor
ments of 21 C.F.R. 121.1002 [now 21 C.F.R. 172.3
empted by 21 U.S.C. § 348. Leeds-Dixon Laborator
and made proper claim to the seized materials. . . .

"At the outset the court notes that subsection (i
342(a)(2)(C)(i) by which food additives intende
vestigational use by qualified experts are exempted]
plicable to this proceeding: the tablets in question w
dietary supplements, and not for investigational us
prevail on this motion for summary judgment, the c
tablish, in addition to the lack of fact issues, one of s
theories. Specifically, claimant must be able to come
(a)(2) of section 348, [there is in effect, and it and its u
are in conformity with, a regulation issued under
scribing the conditions under which such additive may
avoid definition of this form of L-tryptophan as a foo
to sustain its motion.

"Claimant contends the L-tryptophan is not a foo
the statutory definition since it has been publishe
'generally recognized as safe' [GRAS] list, 21 C.F.R
claimant is entitled to rely upon the publication (the
government does not dispute), then summary judgmen
for claimant. If, however, the government may prop
the regulation is not properly filed, then summary j
propriate as affidavits and answers to interrogatories
istence of a fact issue as to the actual safety of L-t

"There is ample authority to support the propos
regulations have the force and effect of law and are bi
public and the agency until repealed or suspended. .
not contend, and the court does not decide, that viola

182.5915 by the government is a denial of due process of law. *See Service* v. *Dulles*, 354 U.S. 363 (1957); *United States ex rel. Accardi* v. *Shaughnessy*, 347 U.S. 260 (1954). Not every violation by an agency of its own regulation rises to the level of a constitutional deprivation. *Otero* v. *New York City Housing Authority*, 344 F. Supp. 737, 745 (S.D.N.Y. 1972). It is, however, a correctible breach of duty. *Id.* The court finds that claimant was entitled to rely upon the cited publication, and that use of the L-tryptophan was proper. It should be noted that this case presents the unique situation of the agency disclaiming the validity of its own regulation due to a simple error. There are procedures available to change the substance of the regulation. Until that is done, the claimant is entitled to rely on the notice as published. For the moment, the court may not rely on Mr. Ronk's representation, no matter how accurate, that a change is forthcoming. Until a change is published, it is without legal force and effect.

"Since claimant's use of L-tryptophan is proper and authorized by regulation within the meaning of 21 U.S.C. § 348(a)(2), there is no need to deal with the government's argument based on 21 C.F.R. 172.320.

"The motion for summary judgment is granted."

The article was ordered released to the claimant and judgment was entered in favor of the claimant. However, the *Code of Federal Regulations* was corrected and L-tryptophan was removed from the published list of GRAS products. (F.D.C. No. 62048; S. Nos. 77-88-679/80; N.J. No. 12)

ANIMAL FEED

Beef, ground, frozen, three seizure actions, at St. Joseph, W. Dist. Mo.; Jefferson, W. Dist. Wis.; and Fort Dodge, W. Dist. Iowa.

Charged 9-5-80, 9-30-80, and 9-11-80: when shipped by Monfort of Colorado Inc. (Inedible Meat Products Div.), Greeley, Colo., the article, labeled in part "Frozen Ground Mechanically Deboned Beef For Further Processing By Heat Sterilization Only Not For Human Food . . . Packed For Pet Foods . . . Modesto, Calif.," contained the nonconforming new animal drug diethylstilbestrol, and no approval of a New Animal Drug Application was in effect with respect to the drug's use and intended use; 402(a)(2)(D).

The article was claimed by the shipper who denied the charge. The Iowa and Wisconsin actions were removed and consolidated with the action in the Western District of Missouri.

The claimant represented to the court that the deboned beef was fit for dog food in every respect and did not contain diethylstilbestrol; and that, due to the small economic value of the beef and the substantial storage and legal expenses needed to establish the claimant's position, the claimant had concluded that it would be economically wasteful to contest the actions. Accordingly, the claimant consented to the destruction of the seized articles without a finding of adulteration and agreed to pay all costs and fees associated with the seizure and destruction of the articles. A consent decree ordered the articles destroyed. (F.D.C. Nos. 62954, 63083, 63151; S. Nos. 80-183-628, 80-201-743, 80-125-487; N.J. No. 13)

DRUGS/Human Use

Allopurinol tablets, and **other specified drugs,** at Brooklyn, E. Dist. N.Y.

Charged 11-4-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the District of New York for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 63170; S. No. 80-139-448; N.J. No. 14)

Allopurinol tablets, and **other specified drug stocks,** at Ft. Lauderdale, S. Dist. Fla.

Charged 6-24-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). Default decree ordered destruction. (F.D.C. No. 63006; S. No. 80-239-225 et al.; N.J. No. 15)

Amygdalin tablets, and **amygdalin for injection,** at San Francisco, N. Dist. Calif.

Charged 9-11-78: when shipped by Chemisches Labor Heinrich Kaden, Hamburg, West Germany, the articles, labeled in part "Chemisches Labor Heinrich Kaden . . . Mandelonitril-beta-gentiobioside- B 17—tablets [or 'vials']," were new drugs without effective approved New Drug Applications, and were not exempted pursuant to the court order in *Rutherford* v. *United States*, since the articles were offered for entry into the United States for warehousing in a Foreign Trade Zone and not solely for the personal use and benefit of any particular person who had executed an affidavit accompanying the articles; 505(a).

The articles were claimed by Cyto Pharma U.S.A., Los Angeles, Calif., who denied the charge and asserted that the FDA was enjoined from impeding and preventing the importation of the articles. The claimant also argued that drugs within the San Francisco Free Trade Zone were exempted from American food and drug laws. The claimant served requests for admissions on the government. The government served written interrogatories on the claimant.

The government moved for summary judgment, and the claimant cross-moved for summary judgment. At the summary judgment hearing, the court requested the parties to obtain information regarding the Free Trade Zone in order to determine whether an order might be made permitting the unlicensed drug to be held at the Free Trade Zone and released only upon presentation of affidavits in compliance with the procedure authorized in *Rutherford* v. *United States*. Upon application of the government, the proceedings in this case were stayed until final disposition by the Supreme Court of the *Rutherford* action. Subsequently, upon the court's own motion and for the reasons set forth in

United States v. *Rutherford*, 442 U.S. 544 (1979) and *Rutherford* v. *United States*, 616 F.2d 455 (10th Cir.), *cert. denied*, 101 S.Ct. 336 (1980), the articles were ordered forfeited and were ordered delivered to FDA for destruction. (F.D.C. No. 61892; S. Nos. 78-150-141½; N.J. No. 16)

Chlorthalidone tablets, hydroxyzine HCl tablets, allopurinol tablets, diethylpropion HCl tablets, furosemide tablets, hydroxyzine pamoate capsules, and **trimethoprim with sulfamethoxazole tablets,** at Detroit, E. Dist. Mich.
Charged 2-15-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper who denied the charge. The action was consolidated for trial with a similar action in the Eastern District of Michigan. Subsequently, pursuant to stipulation, the action was transferred to the District of New Jersey for trial with a similar action there. Ultimately, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62821; S. No. 80-208-574; N.J. No. 17)

Diethylpropion HCl tablets, and **other specified drugs,** at Ferndale, E. Dist. Mich.
Charged 3-21-79: when shipped by Pharmadyne Laboratories Inc., Hackensack, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the Eastern District of New York for consolidation for trial with a similar action. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 62207; S. No. 79-182-135 et al.; N.J. No. 18)

Furosemide tablets, at Philadelphia, E. Dist. Pa.
Charged 10-8-80: when shipped by Superpharm Corp., Central Islip, N.Y., the article was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (F.D.C. No. 63211; S. No. 80-228-093; N.J. No. 19)

Furosemide tablets, and **other specified drug stocks,** at Miami, S. Dist. Fla.
Charged 5-8-81: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications—505(a); and while held for sale, the labeling of the articles lacked adequate direction for use and were not exempted due to their new drug status—502(f)(1). Default decree ordered destruction. (F.D.C. No. 63431; S. No. 81-239-927 et al.; N.J. No. 20)

Hydroxyzine HCl tablets, at City of Commerce, C. Dist. Calif.
Charged 6-13-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the article was a new drug without an effective approved New Drug Application; 503(a). Default decree ordered destruction. (F.D.C. No. 63055; S. No. 80-245-421; N.J. No. 21)

Hydroxyzine HCl tablets, and **furosemide tablets,** at Philadelphia, E. Dist. Pa.
Charged 3-6-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the District of New Jersey for consolidation for trial with a similar action. Ultimately, a consent decree ordered the articles destroyed. (F.D.C. No. 62768; S. No. 80-230-993 et al.; N.J. No. 22)

Hydroxyzine pamoate capsules, at City of Commerce, C. Dist. Calif.
Charged 6-16-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (F.D.C. No. 63063; S. No. 80-245-421; N.J. No. 23)

Metronidazole tablets, at Ferndale, E. Dist. Mich.
Charged 3-6-81: when shipped by Premo Pharmaceutical Laboratories Inc., South Hackensack, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (F.D.C. No. 63346; S. No. 81-185-258 et al.; N.J. No. 24)

DRUGS/Veterinary

Diethylstilbestrol pellets, at Olustee, W. Dist. Okla.
Charged 8-28-80: while held by LaWayne Drury, Olustee, Okla., the article was a new animal drug and no approval of a New Animal Drug Application was in effect with respect to its use or intended use; 501(a)(5). Default decree ordered destruction. (F.D.C. No. 63147; S. No. 80-211-760; N.J. No. 25)

Pig feed medicated supplement, chick grower medicated feed, other finished medicated feed, and **medicated feed premixes,** at Ellendale, Dist. Minn.
Charged 7-15-80: while held by Farmers Milling & Elevator Co., Ellendale, Minn., the articles were being manufactured, processed, packed and held under circumstances that failed to conform with current good manufacturing practice; 501(a)(2)(B). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63104; S. No. 80-217-710 et al.; N.J. No. 26)

Wound dressing aerosol spray, at Blue Springs, W. Dist. Mo.
Charged 4-29-80: when shipped by McRay's Co., Madrid, Iowa, the article, labeled in part "Durvet Scarlet Oil Wound Dressing . . . Biebrich Scarlet Red, Parachloro-Metaxylenol, Methyl Salicylate, Oil of Eucalyptus, Pine Oil, Benzyl Alcohol . . . Hydrocarbon Oil and Propellants 40 percent . . . Manufactured for Durvet, Inc., Blue Springs, Missouri," had been manufactured, processed, packed and held under circumstances that failed to conform with current good manufacturing practice—501(a)(2)(B); and the article was a new animal drug and no approval of a New Animal Drug Application was in effect with respect to its use or intended use—501(a)(5).

The article was claimed by the dealer. The government filed a request for the production of documents, written interrogatories, and requests for admissions. Subsequently, a consent decree of condemnation ordered the article destroyed. However, it was discovered that the spray's propellant was propane (a hazardous substance), and that the spray contained 1,1,1,-Trichlorethane. The court, having been apprised that destruction of the article would require elaborate compliance with applicable toxic and hazardous waste laws and regulations, and would tax the expertise of the office of the U.S. Marshal, found that the proper disposition required the destruction of the article by FDA, and accordingly ordered the responsibility for the destruction of the article transferred to FDA. FDA consulted with the U.S. Marshal and the Environmental Protection Agency and determined that the article could not be destroyed by depositing in a sanitary landfill and that appropriate authorized transportation and disposal at an authorized facility could cost $2,322.85.

In accordance with 21 U.S.C. 334(e), which provides for award of proper expenses against claimants and in accordance with the provision of the consent decree which authorized recovery of subsequently incurred expenses, the government moved for an order taxing additional expenses and directing appropriate transportation and destruction. The claimant opposed such motion and suggested that claimant would gladly pay for the individual discharge of the cans by its employees "into the atmosphere (in a rural setting away from human and animal habitations)" or alternatively by similar "discharge into an open barrel outdoors in such manner that there would be slow absorption in or by the atmosphere." Due to the unforeseeable extent of the costs requested, the court directed the filing of supporting materials and responses.

Ultimately, the court said:

"Pending is plaintiff's motion for costs of destruction. Due to the unforeseeable extent of the costs requested, the court previously directed the filing of further supporting materials and response. Upon review of the materials, it does appear reasonable and necessary that the forfeited articles be disposed of by a licensed disposal facility such as the one contemplated by the government, and that it was reasonably foreseeable at the time the consent decree of 'condemnation and *destruction*' was entered into that costs would be incurred for the destruction. It was not, however, foreseeable . . . that the government would request costs for transportation to a disposal site in the manner now suggested, which sum would be far in excess of any transportation costs which plaintiff has encountered for such products and has not been convincingly shown to be necessary. Even if such a showing of necessity could ultimately be made in a suit for such costs, the consent decree cannot form the basis for that award, and transportation costs awarded will be limited to those which claimant could have reasonably foreseen and which are therefore properly within the scope of its agreement. Accordingly, it is hereby ordered that costs are awarded in favor of plaintiff and against claimant in the amount of $106.05 for handling and disposal of the forfeited articles, and of $148.96 for transporting the forfeited articles to the disposal site. Despite said limitation in the amount of costs awarded for transportation, transportation may be made in any reasonable manner deemed appropriate by plaintiff, at its own cost to the extent that the cost exceeds this award."

Thereafter, the article was transported to and destroyed at licensed disposal facility, in accordance with state, federal and local regulations and laws. (F.D.C. No. 62941; S. No. 80-23-422 et al.; N.J. No. 27)

MEDICAL DEVICES

X-ray control panel, Traceray III, at Evanston, N. Dist. Ill.

Charged 11-9-79: the article, which had been manufactured by Western States Supply, Ltd., Pueblo, Colo., was dangerous to health when used as directed because the article would emit radiation beyond the pre-set exposure time—502(j); the accompanying labeling was false and misleading in claiming compliance with the regulation's standards, and in claiming that the device would deliver the radiation exposure stated in the instruction manual—502(a); and the article's quality fell below its purported quality—501(c). Consent decree authorized release to the possessor for reconditioning. (F.D.C. No. 62648; S. No. 79-151-080; N.J. No. 28)

X-ray control panel, Traceray III, at Manchester, E. Dist. Tenn.

Charged 10-15-79: the article, which had been manufactured by Western States Supply, Ltd., Pueblo, Colo., was dangerous to health when used as directed because the device would emit radiation beyond the pre-set exposure time—502(j); the accompanying labeling was false and misleading in claiming compliance with the regulation's standards, and in claiming that the device would deliver the radiation exposure stated in the instruction manual—502(a); and the article's quality fell below its purported quality—501(c). Consent decree authorized release to possessor for reconditioning. (F.D.C. No. 62642; S. No. 79-131-420; N.J. No. 29)

X-ray control panel with collimator, Traceray III, at Honolulu, Dist. Hawaii.

Charged 10-17-79: the article, which had been manufactured by Western States Supply, Ltd., Pueblo, Colo., was dangerous to health when used as directed because the device would emit radiation beyond the pre-set exposure time—502(j); the accompanying labeling was false and misleading in claiming compliance with the regulation's standards, and in claiming that the device would deliver the radiation exposure stated in the instruction manual—502(a); and the article's quality fell below its purported quality—501(c). Consent decree authorized release to the possessor for reconditioning. (F.D.C. No. 62538; S. No. 79-145-841; N.J. No. 30)

X-ray system, Traceray III, at West Allis, E. Dist. Wis.

Charged 10-5-79: the article, which had been manufactured by Western States Supply, Ltd., Pueblo, Colo., was dangerous to health when used as directed because the device would emit radiation beyond the pre-set exposure time—502(j); and the article's quality fell below its purported quality—501(c). Consent decree authorized release to possessor for reconditioning. (F.D.C. No. 62527; S. No. 79-188-131; N.J. No. 31)

X-ray systems, Traceray III, two seizure actions, at Knoxville, E. Dist. Tenn., and Oneida, E. Dist. Tenn.

Charged 10-12-79 & 10-12-79: the articles, which had been manufactured by Western States Supply, Ltd., Pueblo, Colo., were dangerous to health when used as directed because the devices would emit radiation beyond the pre-set exposure time—502(j); the accompanying labeling was false and misleading in claiming compliance with the regulation's standards, and in claiming that the devices would deliver the radiation exposure stated in the instruction manual—502(a); and the articles' quality fell below their purported quality—501(c). Default decrees ordered disposal of the articles in accordance with the statute; however, the possessor, Interstate Medical Products Inc., filed a claim for remission and prayed for release under bond for reconditioning. The court ordered such release and the articles were brought into compliance. (F.D.C. Nos. 62640, 62641; S. Nos. 79-228-891, 79-228-892; N.J. No. 32)

X-ray systems, Traceray III, two seizure actions, at Phoenix, Dist. Ariz., and Camp Hill, M. Dist. Pa.

Charged 10-3-79 & 10-16-79: the articles, which had been manufac-
tured by Western States Supply, Ltd., Pueblo, Colo., were
health when used as directed because the devices would en
beyond the pre-set exposure time—502(j); the accompany
was false and misleading in claiming compliance with the
standards, and in claiming that the devices would deliver t
exposure stated in the instruction manual—502(a): and
quality fell below their purported quality—501(c). Default
dered destruction. (F.D.C. Nos. 62579, 62631, S. Nos. 79-
204-614; N.J. No. 33)

Notices of Judgment are given pursuant to section 705 of
Food, Drug, and Cosmetic Act. Notices of Judgment report cas
seizure proceedings, criminal proceedings, and injunction p
Seizure proceedings are civil actions taken against *goods* alle
violation, and criminal and injunction proceedings are agai
individuals charged to be responsible for violations. The cas
involve foods, drugs, devices, or cosmetics which were alleged
terated or misbranded or otherwise violative of the law when
into and while in interstate commerce, or while held for sale aft
in interstate commerce.

Notices of Judgment are prepared by Food and Drug Divi
of the General Counsel, HHS.

Published by direction of the Secretary of Health and Huma

Arthur Hull Hayes Jr., M.D., *Commissioner of Food*
Washington, D.C., M

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Section 705[375] of the Food, Drug, and Cosmetic Act: (a) The Secretary shall cause to be published from time to time reports summarizing all j
decrees, and court orders which have been rendered under this Act, including the nature of charge and the disposition thereof.
(b) The Secretary may also cause to be disseminated information regarding food, drugs, devices, or cosmetics in situations involving, in the opi
Secretary, imminent danger to health, or gross deception of the consumer. Nothing in this section shall be construed to prohibit the Secretary fr
ing, reporting, and illustrating the results of the investigations of the Department.

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Go Ahead, Ask Your Doctor

You've just been handed a prescription. You start to look forward to better health. But what do you know about that drug? Do you understand what it is meant to do? Do you know how to take it? Medicines can have some side effects, and they have to be taken correctly. So, be sure to read instructions carefully, and don't hesitate to ask your doctor about:

- **When to take the medicine.** Some drugs should be taken on full stomachs, some on empty stomachs, some in the morning, some before going to bed.

- **How to take the medicine and how much.** With water, with milk or without anything? Should the dose be one or

- **What not to take with the medicine.** Some medicines don't mix with alcohol, others shouldn't be mixed with other drugs.

- **What side effects the drugs can cause.** Medicines may produce a variety of other reactions. Not all people will have the same side effects but you should know what the possibilities are.

There are many sources of information about prescription drugs. Ask your doctor or pharmacist.

A message from the Food and Drug Administration. For more material about being an informed patient, write to: FDA, HFE-88, Rockville

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At least 70% fewer calories than Giant Food regular Blue Cheese Dressing
Libby's
LITE
PEAR

FDA CONSUMER

VOL. 16 NO. 5 **JUNE 1982**

The Tin of Salmon Had But a Tiny Hole 6
A tiny hole was found in a tin of salmon that was consumed by a Belgian couple who became ill. The man died, setting off a widespread search for other tins containing the holes. This article tells the story of that search.

That Lite Stuff 10
Reduced calorie food is usually called light or lite food. But to wear that identification on the label it must be genuinely reduced in calories.

Sunglasses: They're 'Cool,' They Protect 12
First made popular by aviators some 60 years ago, sunglasses have in recent years been high fashion. But they can also serve to screen out harmful rays of the sun.

Cows Produce It; Man Improves It 16
Milk is both a nutritious and safe food. But it doesn't necessarily come from the cow that way. Nor does it come from the cow in the many varieties that are available these days.

Everyman's (Woman's, Too) Guide to Rx Drugs 21
A primer on prescription drugs, this article gives some helpful information on how and how not to take medicines.

Hypertension Targets: Blacks, Elderly 27
Some 60 million Americans have hypertension, or high blood pressure, but the problem is particularly prevalent among blacks and older citizens. Research shows that salt may contribute specifically to the problem for blacks.

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Notices of Judgment 39

Goodies without guilt. That's the tantalizing promise behind food labels sporting claims such as "diet," "light" and "reduced calorie." In most cases, the products are trimmed of at least one-third of their calories—but read the label to be sure. For a lesson in choosing calorie-trimmed foods, see That Lite Stuff, *page 10.*

Richard S. Schweiker
Secretary, U.S. Department of
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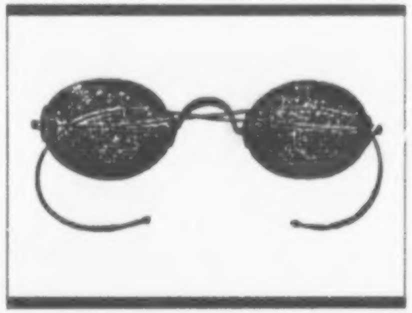
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Updates

Brewing Poison

Antiques are lovely to look at but who would suspect they could be a hazard to health, especially for an economics professor who likes his cup of tea?

The antique caper was a real mystery case, relates Judith D. Rubel, writing in the winter '82 issue of *Lahey Clinic*, the news magazine of the Lahey Clinic Medical Center. The story began to unfold when George Betz, a University of New Hampshire professor, came to the Lahey Clinic, Burlington, Mass., complaining of chills, fever, nausea, unsteadiness, fatigue, headaches and numbness in his fingers and toes. Dr. H. Royden Jones Jr. of Lahey's neurology department ran a series of tests. The results looked suspiciously like arsenic poisoning. Was someone trying to poison the professor?

Tests of Mrs. Betz and the couple's two children showed no trace of arsenic, and checks of well water, possible shellfish poisoning and insecticides were all negative. As the search went on, Jones asked what Betz was using that other members of the family were not. The answer: an antique copper kettle for brewing tea in his study. The kettle belonged to the 17th century house they were renting in Durham, N.H.

The suspect kettle was brought to Boston and tested along with a modern counterpart. Tests revealed that tap water boiled in the antique kettle contained arsenic, while that boiled in the modern kettle did not.

Betz stopped making tea in the antique kettle and was completely recovered in two months.

The moral of the story is that cookware can be a source of food additives, as noted in the March 1982 *FDA Consumer*; however, that article failed to point out that 17th century cookware can also be the source of additives—poisonous ones, at that.

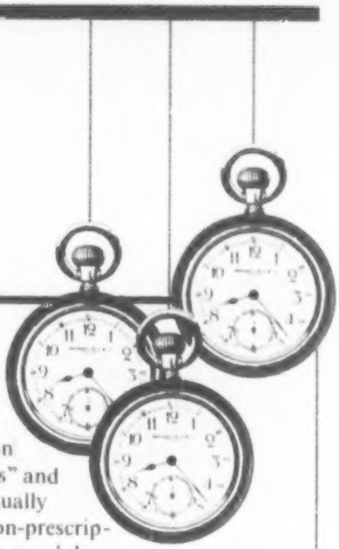
Fungal Products Cited

Consumers spend $60 million a year to treat jock itch, athlete's foot and ringworm, three fungal infections that were discussed in "About the Fungus Among Us" (*FDA Consumer*, May 1982). In March, a panel of experts studying over-the-counter (OTC) drug ingredients for FDA said the following ingredients in OTC anti-fungal medications are safe and effective: iodochlorhydroxyquin, tolnaftate, and the calcium, copper and zinc salts of undecylenic acid. Tolnaftate can also be used to prevent as well as treat athlete's foot, the panel said.

In addition, the panel recommended that three prescription drugs be switched to OTC use. Haloprogin and miconazole nitrate are deemed safe and effective as single ingredients, but nystatin should be used only in combination with other safe and effective ingredients, according to the panel. In the preamble to the panel report, FDA disagreed with the recommended switch of nystatin to OTC use but said no final decisions would be made on the other recommendations until comments on the report had been evaluated. Drug companies could make the switch to OTC for haloprogin and miconazole nitrate now, the agency said, although there is always the possibility the panel's recommendation will not be accepted by the agency.

FDA also disagreed with a panel recommendation that haloprogin, miconazole nitrate and nystatin be marketed over the counter for treating external itching associated with vaginal yeast (candidal) infection. Such conditions must be diagnosed by laboratory tests. Self-treatment of vaginal itching without knowing its exact cause could create a serious health hazard, the agency said.

The suggestion that hydrocortisone or hydrocortisone acetate be combined with other anti-fungal ingredients is not being accepted at this time by FDA. Two



such combinations now on the market have been classified as lacking evidence of effectiveness, the agency pointed out.

The agency will continue to permit the marketing of anti-fungal/antiperspirant combinations and anti-fungal/keratolytic (peeling) combinations already on the OTC market and will permit the reformulation of products to include safe and effective ingredients except where switches from prescription to OTC are involved.

The expert panel found no evidence of safety and effectiveness for nine other ingredients, including camphor, coal tar, menthol, tannic acid and thymol. Further testing was recommended for 24 ingredients, among which were aluminum salts, basic fuchsin, benzoic acid, methylparaben, salicylic acid, sulfur and triacetin.

Looking at anti-fungal drug labeling, the panel said claims such as "treats athlete's foot," "cleans up tinea pedis (athlete's foot)" or "kills ringworm fungi" would be acceptable. What labels can't claim, among other things, are that the product works "fast," "speeds healing" or "kills athlete's foot on contact."

Users should be warned not to use anti-fungal drugs on children under 2. If athlete's foot or ringworm infections don't clear up in four weeks or if jock itch doesn't respond in two weeks, a doctor should be consulted. People should also be aware that OTC anti-fungal products are not effective against ringworm of the scalp or nails.

The report by the Advisory Review Panel on Over-the-Counter Antimicrobial Drug Products was published in the March 23 *Federal Register*. Ninety days were allowed for public comment. After the report itself and the public comments have been evaluated, FDA will issue proposed standards for acceptable ingredients and labeling for anti-fungal drug products. Once the standards are issued in the form of a final regulation, all anti-fungal products must conform to the standards or be removed from the market.

More on Fake Drugs

FDA has requested that Bill R. Frye be held in contempt of court because he continued to sell look-alike drugs such as those seized at his firm, Frye Pharmaceuticals Inc., Birmingham, Ala., last September.

Look-alike drugs are similar in appearance to abused substances commonly sold on the street. Instead of "uppers" and "downers," however, they usually contain a combination of non-prescription drugs such as caffeine, a nasal decongestant and an appetite suppressant.

The motion for contempt was filed on Feb. 24, 1982, after an investigation by the Drug Enforcement Administration revealed that Frye sold illegal capsules in January that were the same as those seized by U.S. marshals on Sept. 30, 1981. The motion was filed in the U.S. District Court for the Northern District of Alabama.

The seizure of fake pep pills at Frye Pharmaceuticals was one of nine seizures made last September at look-alike drug factories in New York, Illinois, Pennsylvania, Florida and Alabama. At the request of FDA, U.S. marshals seized both the counterfeit drugs and the equipment used in making them as part of a nationwide effort to stop the production of the look-alikes. (See "On the Trail of Counterfeit Drugs," *FDA Consumer*, December 1981-January 1982.)

Frye Pharmaceuticals entered into a consent decree of permanent injunction and condemnation on Oct. 23, 1981. Under the terms of the court order, Frye and his firm were permanently enjoined from manufacturing, distributing or promoting any counterfeit drugs.

Drug for Herpes

The first drug to help manage genital herpes has been approved by FDA. The product, acyclovir ointment, has been shown in tests to shorten episodes of the disease, though not to cure it.

Genital herpes, which was discussed in a November 1981 *FDA Consumer* article titled "Herpes Thrives on the Sexual Revolution," affects between five and 20 million Americans. It is caused by the herpes simplex type 2 virus, and occasionally by herpes simplex type 1, which commonly produces cold sores in the mouth and on the lips. Both herpes viruses can be transmitted through sexual contact.

Many victims of genital herpes continue to suffer attacks following the initial infection, while others rarely or never have follow-up attacks. Acyclovir was tested both on patients with initial infections and those suffering recurring attacks. Other forms of the drug besides ointment are still under study.

Female patients with *initial* infections of genital herpes had speedier healing of sores and reduced virus growth when treated with acyclovir ointment, but no significant decrease in pain associated with the disease. In male patients participating in the tests, there was a significant decrease in healing time of sores and in pain. However, in both men and women with *recurrent* genital herpes, acyclovir did not show important benefits.

Acyclovir ointment is also approved for use in patients with herpes attacks resulting from the suppression of their immune systems, as in cancer chemotherapy. It was found to reduce significantly the multiplication of viruses in these patients and to reduce duration of pain.

The ointment is marketed under the trade name Zovirax by the Burroughs Wellcome Co., Research Triangle Park, N.C. The United States is the first country to approve acyclovir for management of herpes. The drug was approved by FDA in eight months.

Genital herpes infections appear to have occurred at epidemic proportions between 1966 and 1979, according to a report by the U.S. Centers for Disease Control. (1979 is the last year for which figures are available.) Half a million new cases of genital herpes are estimated as occurring every year in the United States.

Snake Venom Enjoined

The Miami Serpentarium Laboratories Inc., its owner William Haast, and his principal assistant Nancy Harrell have been permanently enjoined from making and distributing PROven, a snake venom product promoted by the serpentarium for treatment of multiple sclerosis, arthritis and other illnesses. The story of Haast and his involvement with snake venom was told in "Snake Venom a Medicine? No Proof Yet" in the September 1981 *FDA Consumer*.

The March 30 order by Judge Joe Eaton of the U.S. District Court for the Southern District of Florida ends efforts by the government to get the serpentarium to adequately manufacture and test PROven before distributing it to the public. Experts attending an FDA-sponsored public workshop on snake venom in November 1979 concluded that PROven had not been standardized and characterized by laboratory testing to an extent adequate to allow preliminary clinical testing, let alone commercial distribution.

Nonetheless, the serpentarium continued to manufacture and distribute the snake venom product to persons who then used it without medical supervision. FDA wrote to the serpentarium in September 1980 requesting that the laboratory cease making PROven because of concerns that the product is potentially toxic, that the venoms weren't tested for sterility, that variations in venom content were found from batch to batch of the product, that even different venom types were used, and that the final product wasn't properly tested and lacked the necessary licenses.

When Haast failed to comply with FDA's request, the agency in October 1980 petitioned the court to order the laboratories and principal officers to comply with the federal law. Judge Eaton issued a preliminary injunction on Jan. 16, 1981.

Controls on Infant Formula

The specifics of quality control requirements that manufacturers must follow in producing infant formula were published in the *Federal Register* April 20.

The Food and Drug Administration regulation covers the complete manufacturing process of infant formulas, from the receipt of ingredients until the finished product is released for shipment.

It requires manufacturers to establish a quality control system to verify that required nutrients have been added to each batch of formula during the manufacturing process. In addition, ingredients containing nutrients likely to be affected by shipping or storage will have to be analyzed by the manufacturer for proper nutrient content before use in the formula.

Another key element of the regulation requires manufacturers to test for nutrient levels before shipment of finished infant formula products. Samples of the finished products also must be kept and tested for nutrient values throughout their shelf life, generally 12 months.

Other elements of the regulation require manufacturers to:

- code each product to tell where and when it was packed.
- notify FDA 90 days before introducing a new

infant formula so that the proper nutrients and quality control can be assured by the agency.

- assure FDA that the products were processed according to their own quality control procedures.
- tell FDA when they have reason to believe their products may be deficient in the required nutrients.

Quality control records must be kept by manufacturers for one year beyond the expected shelf life of the formula and made available to FDA upon request. This would aid in the identification of any batch of infant formula that did not contain the required nutrients or might otherwise present a health risk.

The events leading up to the new infant formula regulations were the subject of "Next to Mother's Milk, There's Infant Formula," in the July-August 1980 *FDA Consumer*. How a young mother made herself heard on the matter of defective formula was told in "How Consumers Get Activated" in the November 1980 *FDA Consumer*.

Hope for Acne Victims

Most acne sufferers can successfully treat themselves with non-prescription lotions, creams and gels that contain sulfur or benzoyl peroxide or combinations of sulfur with either resorcinol or resorcinol monoacetate, according to a report to FDA by an expert medical panel.

Although it judged sulfur and benzoyl peroxide safe and effective for treating acne and preventing new acne lesions, the panel said products that combine the two should be made available only by prescription and should be used carefully, according to a doctor's instructions. Both ingredients are skin irritants. Resorcinol alone was not found effective by the panel.

Two other ingredients, povodine iodine and salicylic acid, need further testing to establish their safety and effectiveness, according to the panel. Twenty-three ingredients, including benzocaine, camphor, coal tar, thymol, vitamin E and zinc salts, should not be used in acne medications, the panel said.

The expert panel also looked at the labeling of products for acne treatment and agreed that acceptable claims could include such phrases as "for the management of acne," "anti-acne medication" or "unplugs pores to help clear acne." Unacceptable labeling claims include "promotes healing," "fights acne pimples," "dries up excess oils" or statements suggesting the product acts fast.

Products containing benzoyl peroxide should include a label warning not to use the product on sensitive skin. Labels on sulfur-containing acne preparations should warn users against letting the drug get into the eyes.

Acne affects about 80 percent of all adolescents, as well as some older persons. It cannot be cured but can be successfully treated with the proper non-prescription drugs by more than three-fourths of the people suffering from it, the panel said. However, some severe cases require prescription drugs used under the supervision of a physician.

Although abrasive scrub products are useful to wash oily secretions off the skin and to keep pores open, the panel said these products have no effect on acne lesions.

The panel said there appears to be no convincing evidence that chocolate or "junk foods" cause acne or make it worse. How acne gets its start and how it is treated by doctors was explained in "Stubborn and Vexing, That's Acne" in the May 1980 issue of *FDA Consumer*.

The report on acne was prepared by the Advisory Review Panel on Over-the-Counter Antimicrobial Drug Products, made up of non-government medical and scientific experts, as part of FDA's ongoing evaluation of active ingredients in OTC drug products. The panel's report was published in the March 23 *Federal Register* with 90 days allowed for public comment.

FDA, after evaluating the panel's recommendations and the comments received, will propose standards for acceptable ingredients and labeling of acne drug products. Once the standards are issued in the form of a final regulation, all acne products must conform to the standards or be removed from the market.

Correction on PPI Item

An Update in the March 1982 *FDA Consumer* incorrectly portrayed the status of FDA's test program for patient package inserts. The agency proposed on Feb. 19 to rescind this program, which had been established in September 1980. The comment period expired on April 20. As of this writing, the agency has not made a final decision about this program.

The deserted shedlike cannery buildi
bring the salmon from the tenders,
troughs to convey them by species to
Swede pointed out the complicated mach

"In the old days they shipped up Ch
Chink takes no more than a second fo
break down and the foreman has to s
machines are worth."

They followed the roller belts to t
knives and hoses would be cleaning th
the filler machines, with chutes feeding
down the flattened cans that were op
the fish and put the pieces in the can
Hank, "one-pound talls and half-pound
pack that day. Everything's got to be p
the whole summer. That includes nails,
months, all the diesel for our 20 seiners
it takes a month to get anything up from

"Just of empty cans you must need tho

"Thousands? That ship's bringing in sev

"Come on."

"We'll process about a hundred thir
fish an hour for each of the two lines
twelve-hour day. One of those filler m
cans a minute. One gets jammed and th
is water, fresh water everywhere. Except
flow is everything. You need deep enou
strong enough to take off a million fish
and inspectors who can shut down yo
you've got to take time from whatever yo

"Do we have anything to hide?"

"No, but they treat you like you do.
through the weighing machine, and an
the patching table. A one-pound tall
salmon, like it will say on the label. The
out the weight."

They continued down the line to th
and a lid that remained slightly loose.
or vacuum sealer, which pulled down
operation the cans were stacked on big
cooking machines, called retorts. "They
minutes at two hundred forty degrees.
had to boil the cans in water for six or

ngs were cavernous. There was the fish elevator to
the bins to store them, the sorting belts and sluice
the indexers for heading, and then the Iron Chinks.
ines.
inamen to do the butcher work. Now the Iron
all the guts, scales, fins. Sometimes the Chinks
et up a hand line. Then you'll see what those

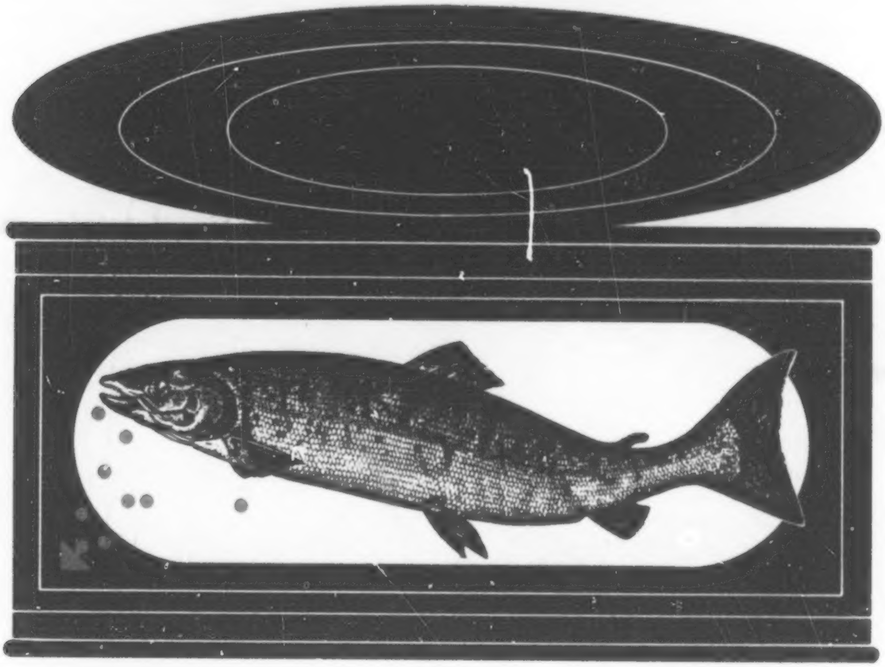
he sliming tables, where people with brushes,
e carcasses coming from the Chink. Next came
into them from the ceiling. The chutes brought
ened automatically, while parallel blades sliced
s. "You'll have two sizes of cans," Swede told
flats, and you decide ahead what you want to
planned. Last January I made out my order for
lumber, salt, cans, food for 140 people for two
and the others who fish for us. You run short,
Seattle."
usands."
enteen million cans."

ty thousand pinks a day, that's five thousand
more than three hundred thousand cans in a
nachines opens and fills a hundred twenty-five
e whole line backs up. Another thing you need
for a piece of shore to build on, a heavy water
gh harbor for the boats and tenders, and tides
theads. We have sewage treatment now by law,
our plant. They fly in when they please, and
u're doing."

Okay, look here. The open cans full of fish pass
y that are underweight divert automatically to
has to contain fifteen and a half ounces of
patchers stick in another piece of fish to round

clinchers that put a code number on the can
The cans then passed through the exhaust box
vacuum and made the final seal. In the last
mobile trays called coolers and rolled into the
cook by steam, under pressure, about eighty
That kills all the bacteria. In the old days you
seven hours, and that meant you couldn't turn

The Tin Of Salmon Had But A Tiny Hole



Among the several thousand cans that went through one salmon cannery on a July day in 1980 was a production lot of half-pounders that the clincher stamped HK13A/Q708 as it sent them on to the sealer and retorts.

And in that lot of 24,000 cans was one with a tiny puncture mark (later covered by the label) that has allowed botulinum spores to enter and to grow. A year and a half later that can would cause the death of a young father in Belgium, celebrating with his wife their child's first birthday.

That incident would lead to examination of the entire 1980 and 1981 output of the Alaskan salmon industry, the discovery of additional defective cans, and a series of recalls involving 50 million cans, the second largest group of food recalls in FDA history.

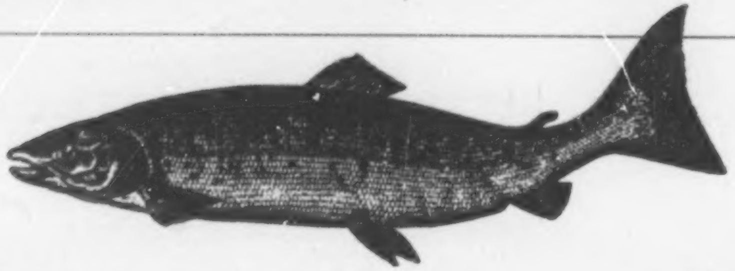
Here is the chronology of those February and March events of 1982, told in the order of their occurrence.

Feb. 5. FDA's Rockville headquarters learns that a Belgian couple has been hospitalized with a suspected case of type E botulism, a type usually associated with fish and seafood. The apparent source is a John West (English label) can of pink salmon packed in Alaska, found in a trash box in the couple's home. The lid with its identifying marks is missing, but the can label is matched to others like it in the store where it was purchased. The lot number on those lids is HK13A/Q708. FDA's emergency operations staff alerts the agency's Seattle office, whose district includes Alaska.

Feb. 6. Seattle decodes HK13A/Q708 as pink salmon from a Ketchikan cannery, regular pack, 7¾ oz., first shift; 24 July 1980, seine catch. Seattle records show that FDA had inspected that cannery July 29, 1980, and had checked production reports at the time dating back past the 24th, with no problems noted on the 24th. The HK13A lot consisted of 24,384 cans; the packer was NEFCO-Fidalgo.

Feb. 7. The husband has died, the wife is recovering. FDA tells the U.S. Embassy in Brussels that antitoxin for type E botulism is available in Sweden and the United States if this is more than a single incident. FDA also asks for details on Belgian test and laboratory methods, examination of can and contents, etc. Warnings on eating John West brand salmon are broadcast throughout Belgium and over the U.S. Armed Forces Radio Network for English-speaking people stationed there.

Feb. 8. The lid has been located and is stamped HK13A. This confirms that the can came from that lot. Unfortunately, the lid has been washed clean and cannot be tested for botulinum. U.S. Embassy staffer Mary McDonnell, who has seen the original can in the Belgian laboratory, tells FDA headquarters by phone that there is a "small, dented-in black spot and tiny hole" near the bottom seam. Meanwhile, the labeled distributor, John West of Liverpool, reports that shipments of the HK13A lot went to Belgium, the Netherlands and South Africa. John West is recalling all these cans. Belgian officials are testing four cans with the HK13A marking and four (for comparison) with another code, all taken from retail stocks. Back in the United States, FDA's Seattle office reports that NEFCO-Fidalgo's Ketchikan plant packed 8.5 million cans of



salmon in 1980 (a good salmon year) in half-pound (7¾ oz.) and one-pound (15½ oz.) cans. The cans were shipped "bright" (unlabeled) to warehouses in Seattle and Anacortes, Wash. (a thousand miles south of Ketchikan), where they are stored and then labeled as wholesale buyers take them in lots. The John West label was applied at the Seattle Salmon Terminals before being shipped out. FDA's Seattle office describes the Ketchikan plant as a 1920s wood-and-concrete structure used only to pack salmon during the six- to eight-week season. It has had no processing violations in recent years. The National Food Processors Association (NFPA), representing salmon industry interests, tells FDA that the American Can Co. supplied the flattened half-pound cans (flats) and re-forming equipment used at Ketchikan.

Feb. 10. An FDA canning expert, Frank Barnes, flown to Belgium when the incident was first reported, has found that the salmon was made into a pâté by the Belgian couple. He reports that an extract from that pâté killed test mice in the Belgian health institute laboratory. He also reports that the HK13A can has a small punched-in triangular hole, and that bits of salmon still in the can showed many spores when

Feb. 12. Barnes reports that Belgian officials have impounded the various cans and records, but that he will have access to clinical documents and other evidence.

Feb. 15. English health officials, aware of the John West recall and the Belgian incident, advise the public not to use any half-pound cans of U.S. salmon they may have and to return them to the place of purchase. This follows discovery of a returned can of salmon with the same punched-hole defect as found in the Ketchikan product, but packed by another Alaska cannery. The threat, it's now clear, is no longer limited to cans coming out of Ketchikan. Back in the United States, FDA's Seattle office has begun an examination of the 1980 pack stored in the Seattle Salmon Terminals warehouse, the production of packers using American Can Co. re-forming machines, the apparent source of the problem.

Feb. 16. Additional codes have been added to the original (and fatal) HK13A code. All are on defective cans returned by consumers in Belgium. That country reissues and expands its warnings on U.S. salmon; now none of it is welcome. Unilever, an English food importing firm, reports that two defec-

FDA's Seattle staff has found a defective can in the NEFCO-Fidalgo salmon stored in the Terminals warehouse. It is not from the original HK13A run at Ketchikan, but from other production runs there. This means all lots of Ketchikan packed half-pound cans are suspect, and that there may be distribution in the United States. Of that original HK13A lot, it is learned that some was shipped to Poland in food relief packages. The Polish government is notified.

Feb. 17. FDA investigators have been at the Ketchikan plant for two days. The cannery was quickly reopened so that equipment could be checked. FDA engineer Norman Wong has been able to duplicate the malfunction that caused the hole at the rim of some cans. The source was the re-forming machines that spin the flattened cans open at the rate of two a second. After they are opened, the cans go to the machine that places the bottom on them. But some cans were torn by the re-former, causing a tiny hole. These cans would not be truly sealed because of the holes. Even though the filled cans were then properly cooked and sterilized, bacteria (*Clostridium botulinum*) could enter those with the hole as they are cooling. (This bacteria is naturally present everywhere, but only becomes dangerous if it can grow in an oxygen-free environment.) The hole itself might later be sealed by a fragment of salmon, making the can airtight. Then the botulism spores drawn into the can after it was sterilized could grow and form the fatal toxins.

Feb. 18. FDA issues a press release advising U.S. consumers to return to the place of purchase any 7 ¾ oz. cans of salmon, regardless of the label, that have K13 in the code on the lid. Stores and distributors, mostly in the Pacific northwest, clear whatever stocks they have of these codes. FDA's news release also reports the probable cause of the defect, the can re-forming machines, and that NFPA, the food canners trade group, is working with the agency to prevent the recurrence of the problem.

Feb. 19. Canning expert Frank Barnes in Belgium has disassembled one of the defective John West cans and finds that the torn metal at the seam fits the triangular hole. This confirms that the re-forming machines are the source of the problem. Belgian authorities, doing can-by-can checks, have found additional defective cans and are adding more codes to their listing. All are from the Ketchikan plant, and one is from the 1981 pack. Back in Seattle, all FDA investigative personnel have been relieved of other duties for round-the-clock checking of a half million cans in the Terminals warehouse. FDA is also checking the worldwide distribution records of the entire 1980 and 1981 salmon pack of the Whitney (formerly NEFCO)-Fidalgo and Washington Fish and Oyster/Ocean Beauty Seafood firms that distributed all canned salmon from Ketchikan.

Feb. 23. Scattered cans of K13 coded salmon are being returned to retail stores. Apparently, distribution of the suspect code was limited. None show the can defect.

FDA's Seattle office has found 22 defective cans among the half million they have examined. But the problem takes on a new dimension. The 22 cans have code numbers used by other Alaska packers, in addition to NEFCO-Fidalgo. This means the can re-forming machine defect may be common to all Alaska canneries using American Can Co. equipment, and seasons by these packers must be checked.

Alarmed that these recalls and uncertainties are harming public confidence in salmon, NFPA and the salmon industry suggest that they be responsible for checking the 1980 and 1981 salmon packs in warehouse storage, a figure that could go past 20 or 30 million cans. The Seattle office relays this to FDA headquarters, but goes on checking cans that were in the suspect lots. FDA headquarters begins discussing the plan with industry representatives.

Feb. 26. FDA questions some parts of the industry proposal, especially its dependence on "dudding," which is electronically testing cans to see if the vacuum seal is intact. FDA also questions the number of cans to be sampled from each lot; the status of cans already out in distribution channels; and the way that the consuming public will be kept informed of salmon recalls and the overall problem.

March 5. NFPA announces a program agreed to by the salmon industry and FDA to assure the safety of all half-pound cans of salmon from the 1980 and '81 pack, some 50 million cans, most still in Seattle area storage. FDA will monitor the program, which calls for industry to examine all lots of salmon and to demonstrate to FDA that proper quality controls were used in the packing and labeling. If quality control was lacking or a defective can is found, the entire output of that cannery will be recalled from the market. FDA's Office of Public Affairs will announce the recalls and the code numbers as they are made.

March 19. Two Alaskan packers who used American Can Co. machines to form their flattened half-pound cans begin recalling salmon because holes made by the machines were found in some cans. They are Chugach Alaska Fisheries and Diamond E. Fisheries. FDA announces the recall and the codes to be returned. More than 20 million half-pound cans are now being recalled. The agreement FDA negotiated with industry is working.

March 31. Two more Alaskan packers who used American Can Co. machines to form their cans begin recalling from their 1980 and 1981 packs, again because of defects found in the cans. They are Wards Cove Packing and Petersburg Fisheries. Again FDA announces the recall and the many codes involved.

April 8. Whitney-Fidalgo Seafoods is recalling all its 1980 and 1981 packs of half-pound cans produced at the firm's Kodiak and Anchorage plants. St. Elias Ocean Products of Cordova, Alaska, is also recalling half-pound cans from the 1980 and 1981 packs. FDA announces the recall and the codes to be returned.

Date Open. More than 50 million cans of Alaskan salmon distributed throughout the world are under recall. These are from the packers who had defective cans in the warehouses inspected in late February by FDA's Seattle office or were identified in the industry program begun March 5. It is almost 20 percent of the 1980 and 1981 output of the Alaskan salmon industry.

Compiled by Richard C. Thompson, a member of FDA's

That Lite Stuff

by Louise Fenner

Pickings are no longer slim for dieters these days. The shelves in the diet sections of supermarkets are now groaning under the weight of new products promising good taste but fewer calories. For today's shedders there are diet versions of such traditional temptations as pancake mixes and syrups, blue cheese salad dressings, pudding, cheese, ice cream, mayonnaise, gravy mixes and chocolate topping—and, should a thirst develop, even beer and wine.

Diet foods aren't new, but the past few years have seen a striking upsurge in their popularity. Health-conscious Americans seem ready for foods that weigh less heavily on their consciences, and food manufacturers are eager to comply. Many products are marketed as "light" or "lite" versions of regular foods—that is, they contain less of such substances as fat, sugar or alcohol (in the case of beer or wine), and they are usually lower in calories. The whole idea is so palatable that light foods and beverages are one of the fastest growing segments of the American food industry.

Consumers may wonder whether these streamlined foods really cut back on calories. To assure that they do, the Food and Drug Administration requires products claiming to be low or reduced in calories to meet specific limits on calorie content. This helps consumers shopping with weight control in mind to choose products that represent genuine calorie reductions.

FDA's rules, which took effect July 1, 1980, apply to any food its maker claims to be useful in maintaining or reducing body weight or calorie intake. The rules do not cover beers and most light wines, since FDA does not regulate the labeling of alcoholic beverages except wines of less than 7 percent alcohol by volume. However, the Bureau of Alcohol, Tobacco and Firearms (BATF) has labeling guidelines that affect light alcoholic beverages.

Under FDA's regulations, a food can be labeled "low calorie" only if a serving supplies no more than 40 calories and contains no more than 0.4 calories per gram (28.4 grams = 1 ounce). To be labeled "reduced calorie," a food must be at least one-third lower in calorie content than a similar food in which calories are not reduced, and it must not be nutritionally inferior to the unmodified food.

Food that is labeled low or reduced calorie must also bear nutrition labeling. Along with nutrients such as vitamins and minerals, the labels must give the calories per serving and the serving size to which the figure relates, expressed in identifiable units of measurement such as a cup, slice, teaspoon or fluid ounce.

Labels of foods that are naturally low in calories, such as mushrooms, are not permitted to use the term "low calorie" immediately before the name of the product. For example, mushrooms could not be labeled "low calorie mushrooms" because it would suggest that they are lower in calories than other mushrooms. They could be labeled "mushrooms, a low calorie food."

Even though some foods such as salad dressing are normally eaten in small amounts and provide relatively few calories, they cannot be labeled "low calorie" unless they contain less than 0.4 calories per gram. For example, a typical blue cheese dressing for dieters contains about 40 calories per one-tablespoon serving, or 2.5 calories per gram. Thus, it is not low calorie. However, the same dressing could be labeled "reduced calorie" since it has at least one-third fewer calories than regular blue cheese dressing, which has 75 or more calories per tablespoon.

If a food label suggests that calories have been cut, it has to back up that claim with numbers. The label must compare the reduced calorie food with an unmodified version of the product, such as: "Reduced calorie fruit cocktail, 40 calories per serving; regular fruit cocktail in heavy syrup, 90 calories per serving." A reduced calorie food that does not smell and taste in all respects like the food for which it is offered as a substitute—for instance, canned pears in unsweetened water as compared with canned pears in heavy syrup—must be labeled with information about any differences that exist. If a standardized food is modified so that it no longer complies with the standard, it cannot simply add the words "low calorie" or "reduced calorie" to its name; the food must be labeled as "imitation" or be called by another appropriately descriptive name.

Since consumers would reasonably expect a food labeled "sugar free" or "sugarless" to be low or reduced in calories, the label must alert them if this is not the case. For instance, a sugar-free candy may contain sorbitol, a sweetener with the same calorie content as sugar. The label would have to state that the candy is "not a reduced calorie food" or indicate in some other way that the product isn't for weight control. In other cases, the label of a sugarless product might warn dieters that it is "useful only in not promoting tooth decay."

A food aimed specifically at diabetics must bear the statement: "Diabetics: This product may be useful in your diet on the advice of a physician. This food is not a reduced calorie food." If the food does offer calorie savings, however, the last sentence may be eliminated. A food cannot be labeled "dietetic" or "diet" solely because it might be useful for diabetics, since this could be misleading to people seeking low or reduced calorie foods.

Before these regulations went into effect, so-called "diet" foods often turned out to have as many calories as regular products. Now an item can be labeled "diet" or "dietetic" only if it meets the requirements for low or reduced calorie foods, or if it is clearly intended for a special dietary purpose other than weight control, such as "for low-sodium diets." Other label terms that imply calorie savings, such as "artificially sweetened," are generally subject to the same restriction.

If the word "light" or "lite" appears on a label, chances are that it means the food is low or reduced in calories. However, "light" can refer to other properties of food besides calories. For example, "light cream" is cream that contains at least 18 percent but less than 30 percent milk fat. Light syrup, which is used in canned fruit, has a certain density due to the amount of liquid and sweeteners used. Light whiskey has been stored in used or uncharred new oak containers. In light (or lite) salt, some or all of the sodium has been replaced by potassium. Light chocolate usually contains milk or cream and is paler in color than dark chocolate.

Consumers can usually determine whether a light food or beverage offers calorie savings by reading the label carefully. Generally if a light product is intended to be useful in maintaining or reducing body weight or calorie intake, it must meet the requirements for low or reduced calorie foods, including labeling information.

Light beers and wines often provide calorie comparisons on their labels, although this is not specifically required by BATF. Under BATF guidelines, a label that boasts of calorie reductions without giving the calories per serving could be considered misleading. As a general rule, a light beer will contain about one-third fewer calories than the regular version produced by the same brewer. This puts many light beers at 95 to 100 calories per 12-ounce serving, although the different brands range from about 70 to 135 calories per serving. Regular white and rose wines run about 65 to 80 calories per 100 milliliters (about 3.5 ounces, or one wineglass). The light versions contain around 50 to 60 calories. Few, if any, light red wines have appeared.

Reducing the calories in beer and wine means cutting down on carbohydrates or alcohol, or both. Light beers average about 3.2 percent alcohol by weight, according to the U.S. Brewers Association, while premiums average about 3.6 percent and ales 4 percent alcohol. A BATF analysis of light beers found that the alcohol content ranged from 1.9 percent to 3.4 percent, with a mean average of 3.0 percent. For light wines, in which alcohol content is measured by volume, 7 percent to 14 percent is the allowable range. Most wines labeled "light" hit the lower end of this scale.

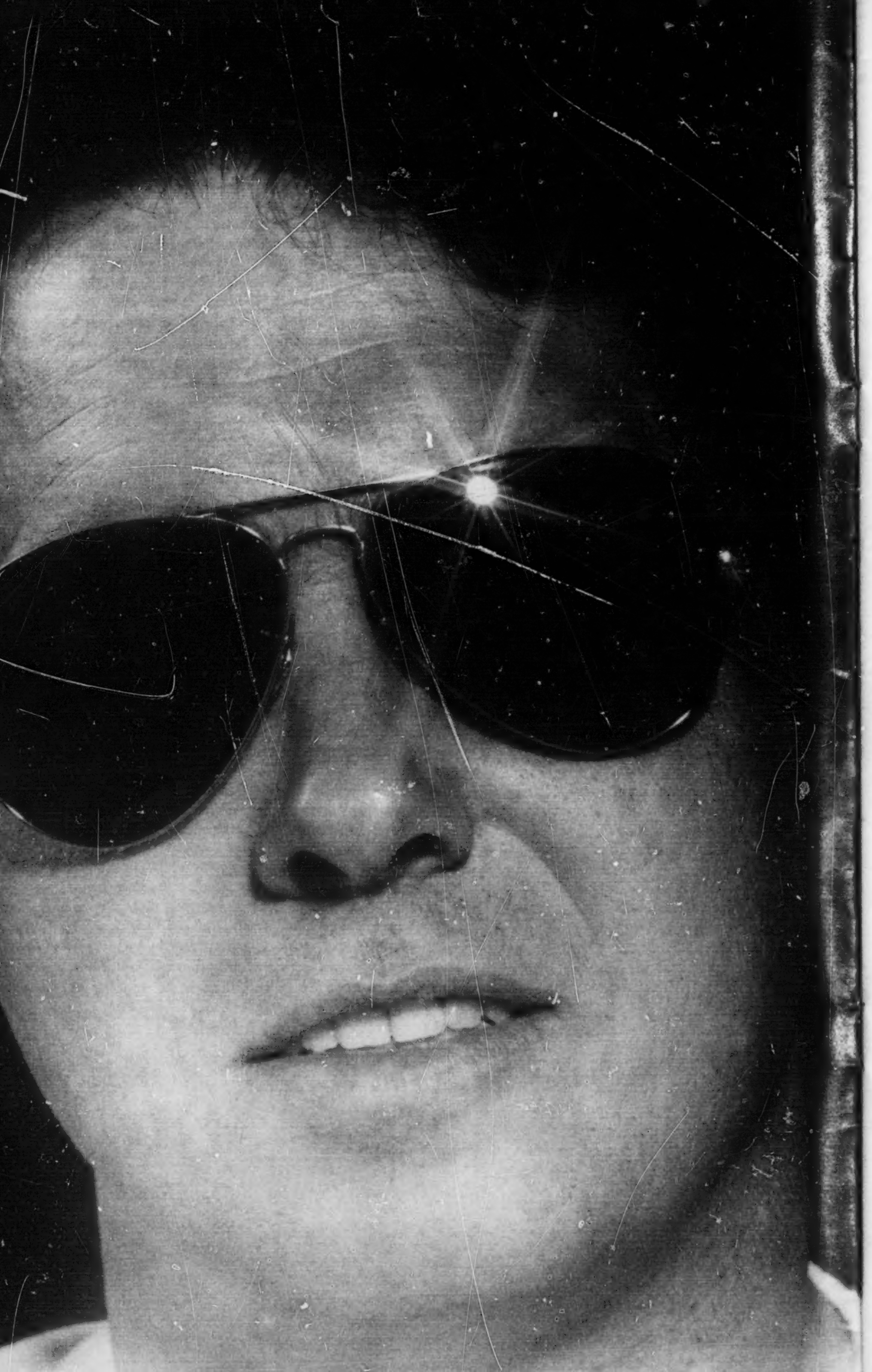
If the alcohol content of a wine is less than 7 percent by volume, the labeling of the product comes under FDA's jurisdiction. The label must indicate that the product is a wine substitute, using such terms as "wine beverage," "winelike product" or "de-alcoholized wine," and it must provide nutrition information and a calorie comparison.

If the surge of inquiries from firms thinking of marketing light foods and beverages is any indication, lightness is here in a big way. In the last year, both FDA and BATF have seen a trickle of calls and letters turn into a steady stream.

For consumers, it means a greater choice of calorie-saving food than ever before. The labels tell the story—and they should be required reading for every smart dieter.

Louise Fenner is a member of FDA's public affairs staff.

SUGAR FREE!
SUGAR FREE!
TaB
Only 1 Calorie per 16 ozs
D-ZERTA
REDUCED CALORIE PUDDING
NO SUGAR ADDED
CHOCOLATE
Diet Delight
APRICOTS
GIANT FOOD
REDUCED CALORIE BLUE CHEESE
At least 70% fewer calories than Giant Food regular Blue Cheese Dressing
ALBA'77
only 70 calories per serving
FIT'N FROSTY
CHOCOLATE FLAVOR
reduced calorie dairy drink mix
the CHOCOLATE TASTE without the CHOCOLATE WAIST
10 ENVELOPES .75 OZ EACH NET WT 7.5 OZ (212 GRAMS)
1/3 fewer calories
MASSON LIGHT
Premium California
LIGHT ROSÉ
PAUL MASSON
Bright Day
DRESSING
Lite
A FINE PILSNER BEER
SUGAR FREE
Cary's
LOW CALORIE SYRUP
12 FL. OZ. 355 LITER



SUNGLASSES

They're 'Cool,' They Protect

by Harold Hopkins

There's a shade of difference in an optimist's and an optometrist's view of sunglasses. If you looked at the world through rose-colored glasses, as optimists are said to do, you might be looking at trouble, the way optometrists see it. They think it's a put-on to put on sunglasses with rose, orange or purple hued lenses, which to them aren't sunglasses really, but fashion wear. Optometrists—as well as ophthalmologists and opticians—know that some sunglasses are made and used for purposes that have nothing to do with the sun, and that some people are more concerned about how they'll look wearing the things than what they can see through them.

In sunglasses made for use in sunlight, optometrists lean to a lens of conservative gray. If you're looking through a medium or dark gray lens, says the American Optometric Association, you won't likely be run in for running a traffic red light you thought was green or amber. Green is almost as good.

For people who spend much time outdoors, particularly around water, snow or sand, sunglasses may be a must. A lot of drivers depend on dark glasses to overcome glare from the highway and other surroundings. In the brightness of winter snow, in the blaze of summer sun on the beach, golf course sundeck or garden, sunglasses can save a person from the blind staggers.

Sunglasses have one primary function. They cut down on the total amount of visible light and reduce daytime glare to give visual comfort. They may also minimize accidents and errors that happen when squinting or eye watering makes seeing difficult.

Some secondary uses: They're *in* as outdoor beach and sports wear accessories. People wear them to mask emotions or thoughts, to hide bloodshot eyes or to enable the wearer to examine nearby persons on the beach or elsewhere without letting them know they're being checked out. Some wear styled sunglasses to change "personality," some to conceal identity. Those who insist on wearing them constantly may be trying to create an air of mystery. Some recent faddists wear sunglasses or eyeglasses pushed back on the head so that they ornament the hair. It's nothing new. Tom Sawyer's Aunt Polly mislaid hers regularly that way.

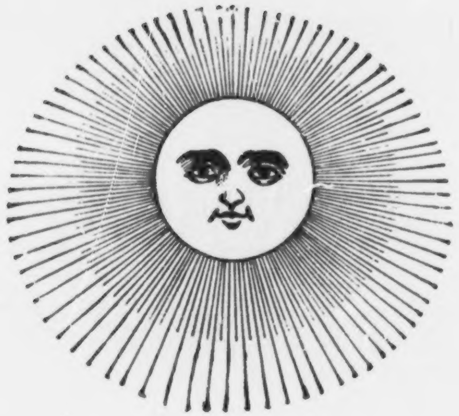
What used to be known as shaded or smoked glasses have been around a long time. George Washington had a pair. Sunglasses even predate prescription glasses, though their popularity didn't become evident until military aviators in the 1920s began donning green-tinted glasses to cope with high altitude glare. The idea caught on slowly at first but has accelerated and exploded in the past several decades. For awhile kids got toy ones in their Crackerjack. Today we're more serious, most of us, about our sunglasses, more discriminating, more concerned with quality, both for safety's sake and good vision. And more of us are wearing them. To some, sunglasses are *de rigueur*, to others functional.

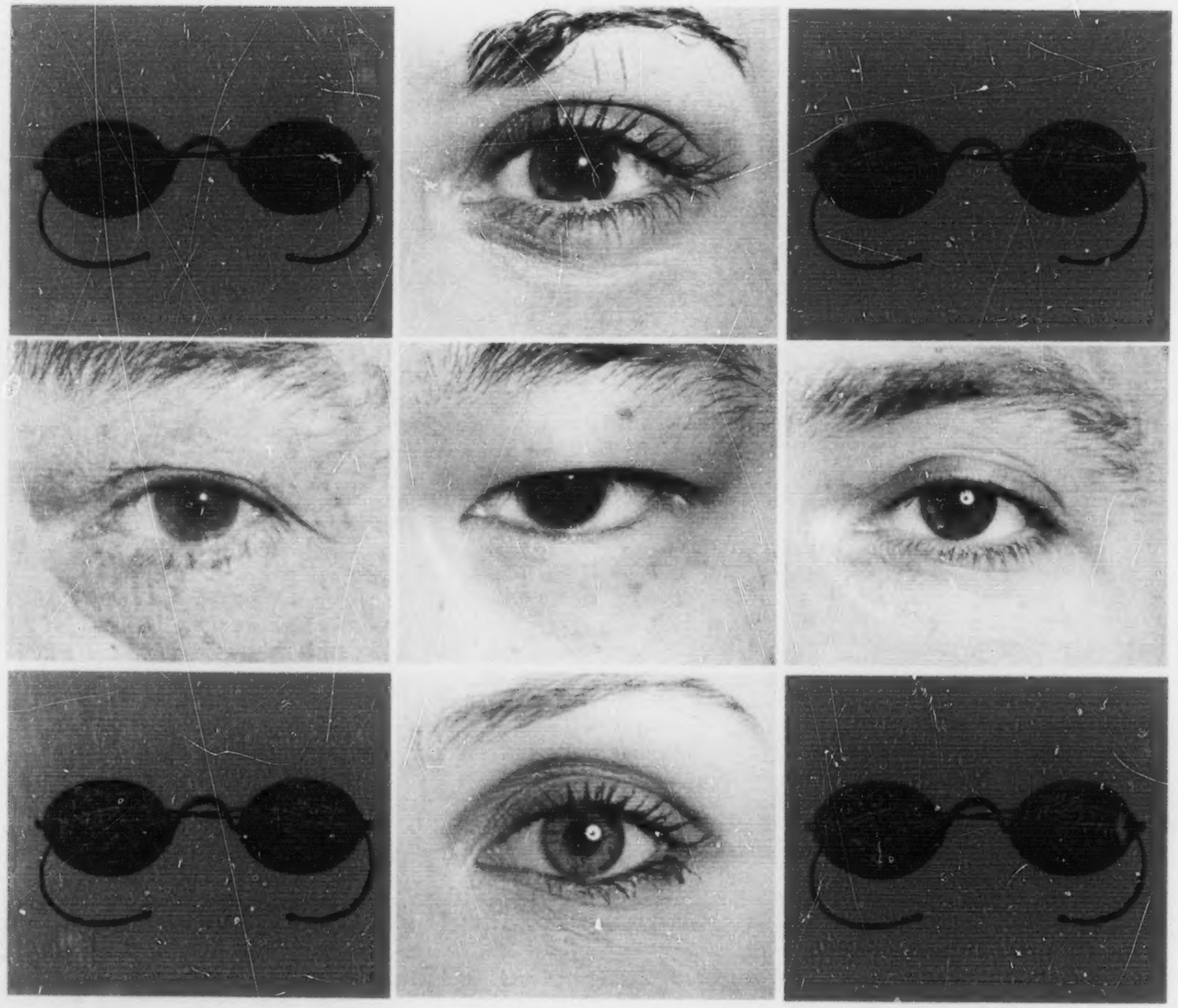
An estimated 86 million pairs were sold in this country in 1980, according to a brochure issued in that year by Corning Glass Works, a maker of a popular type of sunglass lens material that is sensitive to light. Corning said total sunglass sales were $828 million, or $9.63 a pair. A "consumer profile" in the same brochure found that 48 percent of American consumers owned one pair of sunglasses, 31 percent owned two pairs, 12 percent three pairs, 5 percent four pairs, and 4 percent five or more pairs. That's a lot of sunglasses, and it's easy to see why the sunglass racks in drugstores sometimes rival the cosmetics displays.

With the rising popularity of sunglasses, and doubtless because of it, have come changes in design, materials, effectiveness and function. Whereas sunglasses once resembled ordinary eyeglasses with tinted or smoked-glass lenses, today they come in a wide and frequently wild assortment of colors, sizes, shapes, frames and wrap-around contours, with prices to match. They're versatile. Lenses may be of plastic or glass, or combinations, with the light-inhibiting substances mixed into the lens material or coating the lens. Both sunglasses and eyeglasses can be designed, bejeweled and color coordinated to complement the user's dress or play clothes, cosmetics, skin and hair color and facial contours. It's these trends no doubt that have led to appearance of the term "eyewear" in the advertising, fashion and merchandising language of the industry.

This acceptance of sunglasses has been paralleled by advances in the technology of plastics for both lenses and frames which, if one also considers the cosmetic uses, make "sunglasses," technically at least, a misnomer.

Plastic-lensed sunglasses are normally lighter in weight than glass, less likely to shatter from blows or dropping, and don't require the sturdier, somewhat more expensive frames that glass does. But they're more easily scratched and they may not screen out the same amount of ultraviolet (UV) or infrared





(IR) rays that glass lenses will.

Sunglass lenses also may be made of polarizing plastic or "mirrored" coated glass. A development of recent years is a light-sensitive, or photochromic, glass lens that darkens automatically when exposed to outdoor sunlight and becomes lighter in the more subdued light of nighttime or indoors. A photochromic lens of "full" range—that is, one that at its darkest or most opaque will absorb as much as 85 percent of available light and at its clearest or most transparent will hold back only 10 percent to 15 percent of the light—can do double duty, for certain people, as eyeglasses and sunglasses.

Not all photochromic lenses are full range. You'd think this light-to-dark and dark-to-light convenience would be desired only by a person who wears regular prescription glasses. Not so. Photochromic-lensed sunglasses are being sold off the rack, too, and currently are threatening to outsell plastic-lens sunglasses. The question seems to be whether the wearer wants to pay for the convenience of not having to remove the glasses at nightfall or when indoors. Non-prescription photochromic sunglasses are not normally full range, therefore do not darken to the degree optometrists consider necessary for full protection from UV radiation.

Some prescription eyeglass wearers buy sunglasses ground to their prescription. The consumer can have a pair of old eyeglasses tint-coated for use outdoors in the sun—provided, of course, that the prescription is not out of date. Surface tint coatings eventually wear or flake off, however. Those who have contact lenses may add regular non-prescription sunglasses with no trouble. Optometrists advise against wearing tinted or photochromic contact lenses because of the inconvenience and technical problems involved.

Tinted glass lenses may screen out both ultraviolet and infrared rays. Plastic lenses screen out ultraviolet but not infrared rays. Non-prescription polarizing sunglass lenses are made of plastic. They are effective against glare. Prescription polarized sunglass lenses are available but can be expensive, consisting of polarized material sandwiched between layers of clear or lightly tinted glass or plastic. "Mirrored" coated-glass lenses generally screen out more light than tinted lenses do and are intended primarily for intense glare conditions such as skiing. Some "mirrored" lenses, but not all, will screen out both UV and IR rays. Gradient lenses are those that are darker at the top and gradually lighten toward the bottom, permitting the user good visibility nearby but darkening overhead or horizon brightness. Experts say sunglass lenses ought to screen out 75 percent to 90 percent of available sunlight and should be made of a high quality glass or plastic that's impact resistant.

Both sunglasses and eyeglasses are defined as medical devices by FDA. Therefore, they are subject to regulatory requirements for safety and effectiveness, including the impact resistance of lenses. Manufacturers perform tests to assure FDA that their lenses meet impact resistance requirements.

Voluntary industry standards exist for quality, performance and suitability for intended use of non-prescription sunglasses. The industry standards cover freedom of lenses from flaws and faults, ability to transmit and refract (divide) light, and densities. The standards recognize five types of lenses: general purpose, cosmetic, daylight driving, skiing and mountain climbing, and beach and boating.

Called the American National Standards Requirements for Non-prescription Sunglasses and Fashion Eyewear, they were adopted in 1976 under the aegis of the American National Standards Institute. Participating in the standards were ophthalmologists, optometrists, optical manufacturers, the FDA, the National Bureau of Standards, the National Institutes of Health, and the National Society for the Prevention of Blindness.

However, very little of the standards information makes its way to the consumer in advertising or on labels. The consumer is left largely on his own in a highly competitive market. Price ranges aren't helpful as information either, since some of the costs may be for design and cosmetic features. Nor is the optometrist or ophthalmologist apt to have solid information on off-the-rack sunglasses. That information isn't available because reliable testing methods are too expensive and because labels don't normally carry quality or performance specifications.

There have been studies suggesting that some non-prescription sunglasses permit too much UV and IR radiation to reach the eye. Since UV and IR rays are invisible, there is no way the consumer can tell just by looking. Accurate measurement of sunglass lens transmission of UV light requires expensive equipment and testing. One optometrist researcher, Donald G. Pitts of the University of Houston College of Optometry, has suggested, in an article in the *Journal of the American Optometric Association* (December 1981), that sunglass manufacturers adopt lens materials of known UV light-absorbing characteristics. This also would protect especially susceptible groups such as cataract patients and others subject to high exposure to UV radiation. While there are no reports to FDA of problems of this sort, FDA does encourage manufacturers to use materials that block visible and UV light.

The American Optometric Association says "quality" non-prescription sunglasses are those with lenses that are free of distortion, imperfection, and mismatching of color and absorptive power. A simple test is recommended to check refractive quality:

Hold the glasses at arm's length and look through them at a straight line in the distance, such as the edge of the door, while moving the lens across that line. If the straight edge appears distorted, or if it sways, curves or moves, the lens is not optically perfect. Check to see that the coloring in the lens is even and that one lens is not darker than the other. For gradient lenses—those that are shaded so as to become gradually lighter from top to bottom—make sure the lens lightens gradually and in the same areas of both lenses.

Sunglass frames should be large, sturdy and free of rough spots, but the temple pieces shouldn't block side vision. The frames should fit closely enough to remain in place, yet be comfortable on the nose, cheeks, temples and ears. Sometimes frames can be adjusted to fit better by an optician or optometrist.

People differ in their tolerance to bright light and in their occupational and recreational needs, so some need more help from sunglasses than others. Generally, a person should wear sunglasses if bothered by frequent watering of the eyes, squinting or considerable blinking outdoors; if the person spends a lot of time in the sun; or if his doctor of optometry recommends them. Although sunglasses should not be worn at night, wearing them in daytime makes it easier for the eyes to adapt to nighttime darkness, optometrists say.

Harold Hopkins is editorial director of FDA Consumer.

MILK

Cows Produce It; Man Improves It.

by Chris Lecos

It's so easy to take milk for granted. It's produced in such abundance in the United States that supermarket shelves are packed and stacked with an almost bewildering array of milk and milk products. When shoppers go into a store to buy milk, they buy it with confidence. They not only look upon it as a nutritious food but also as a very safe food. And with justification, for milk is one of the best controlled, inspected and monitored of all food commodities.

The abundance of milk and other fluid dairy products so readily available is a result of a key industry's ability to select, breed and feed dairy herds that can provide amazing quantities of milk. A century and a half ago, a dairy cow produced about 1,500 quarts of milk a year. In 1980, the annual average was more than 5,500 quarts, according to the Milk Industry Foundation.

The nutritious qualities of milk have been much heralded and recognized for many years. But there is another side to that coin, too. Not all people are able to drink it regularly because of adverse reactions to lactose (milk sugar) or milk protein. Allergic reactions to the protein are quite uncommon. Lactose intolerance, a condition that requires medical diagnosis to discover, occurs more frequently among some racial, ethnic and other population groups. It is found mainly in countries and cultures where, through the ages, milk and other lactose-containing products have been infrequent parts of the diet after infancy.

The milk that most Americans drink comes from the cow, although goats' milk has its adherents in this country. In some other countries, buffalo, goats, sheep and reindeer are more common milk sources.

In the United States, milk is not only legally defined, but there are also extensive state and local requirements that apply to virtually the whole range of milk production—from the time it is obtained from the cow to its final processing for distribution to the marketplace.

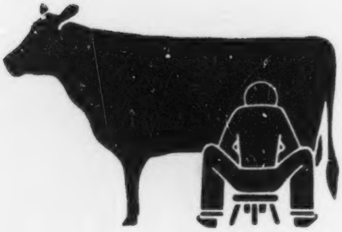
The Food and Drug Administration defines milk in its standards of identity as the lacteal secretion that is "obtained from the complete milking of one or more healthy cows." FDA regulations permit—but do not require—the addition of vitamins A and D to milk and other dairy products. When it is added, at least 2,000 international units of vitamin A must be present in each quart of milk; the minimum amount of vitamin D required as an added ingredient is 400 international units. This means eight ounces of milk would provide about 10 percent of the U.S. Recommended Daily Allowance of vitamin A and 25 percent of the U.S. RDA for vitamin D.

Although the federal government for many years has had established guidelines and recommended standards for milk and milk products, legal responsibility for safeguarding the quality of milk rests with state and local governing bodies. This is accomplished through a network of more than 15,000 state, county and local health and sanitation jurisdictions in the United States, according to the Milk Industry Foundation, a Washington, D.C., based dairy group. The federal standards apply only to milk and milk products that are shipped in interstate commerce (across state lines). Most states also have their own standards for products produced and marketed within their own boundaries. State standards generally conform to the minimum federal standards and, in several states, exceed them.

The packaged milk one buys is a standardized product, but that obviously is not exactly the way it is obtained from a given cow. The composition of raw, unpasteurized milk actually varies from cow to cow and from breed to breed during various stages of lactation and according to the season of the year. The feed, nutrition, age and health of the animal and the condition of its mammary glands also affect the milk's composition. On the average, milk is about 87.2 percent water, 3.7 percent fat, 3.5 percent protein, 4.9 percent lactose and 0.7 percent ash. (The milk fat, protein, lactose and other constituents—except water—constitute what are known as "milk solids.") Milk of varying composition is taken from various dairy farms and is "pooled" at a processing plant. The sophisticated technology employed standardizes the milk to meet the required standards for the types of milk and milk products being produced for consumer use.

Most raw milk from farms is pumped from refrigerated stainless steel tanks into tank trucks for delivery to processing plants. The old 10-gallon milk can is, for the most part, a thing of the past. The truck driver smells the milk for any feed odors—such as wild onion—which has to be deodorized. He also checks the temperature and volume of bulk milk in the farm tank. Samples of raw milk are also collected for analysis before pumping the milk into the vehicle. These samples are analyzed at the processing plants for bacterial count, antibiotics residues, milk fat content and other properties. State and local public agencies also use these samples for their own laboratory analysis.

What most consumers buy in final package form is grade A fluid milk and milk products. Such products, if they are being shipped interstate, must be pasteurized. FDA regulations state that milk can be pasteurized properly if it is heated at one of

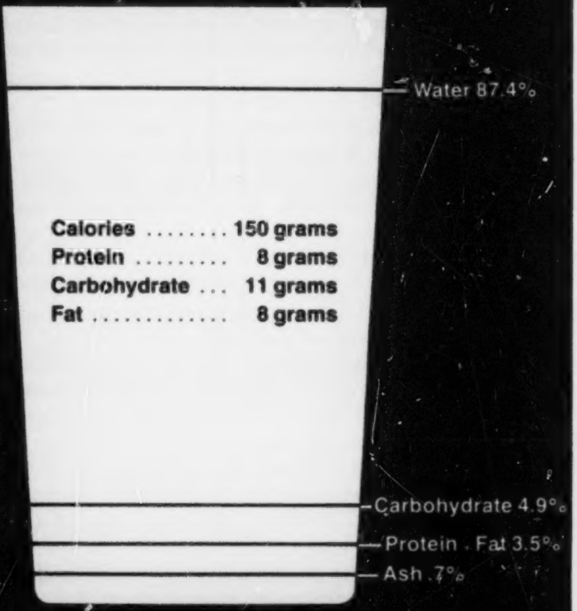


five temperature levels for these lengths of time: At 145 degrees Fahrenheit for 30 minutes; at 161 degrees for 15 seconds; 191 degrees for one second; 204 degrees for .05 second; and 212 degrees for .01 second. If the milk is to be used for a dairy product with a fat content of 10 percent or more or if it is to contain added sweeteners, the temperature levels must be increased by another five degrees, according to FDA guidelines. Thus, in the case of other milk products, cream and chocolate milk, as an example, would be heated to at least 150 degrees for 30 minutes or 166 degrees for 15 seconds. Frozen dessert mixes would be heated to at least 155 degrees and held for 30 minutes or 175 degrees for 25 seconds. The latter products need greater heat treatment because the greater fat and sugar concentrations provide heat resistance to bacteria normally found in milk.

Ultra-pasteurization—minimum heat treatment of 280 degrees for at least two seconds—also is permitted. But the National Dairy Council says it is limited mainly to the production of half-and-half (half cream, half milk), cream, whipping cream and eggnog. Milk that has been subjected to ultra-high temperature treatment is available in some areas of the United States. Sometimes referred to as UHT milk or shelf-stable milk, it is heated at high temperatures, then quickly cooled and aseptically packaged in a sterilized container that is hermetically sealed. The product can be stored unrefriger-

Nutrient Content of Whole Milk

Whole Milk—8 Fluid Ounces
(1 Cup - 244 grams)



Calories	**150 grams**
Protein	**8 grams**
Carbohydrate	**11 grams**
Fat	**8 grams**

	% of RDA
Protein	**20%**
Vitamin A	**4**
Vitamin C	**4**
Thiamine	**8**
Riboflavin	**25**
Niacin	*****
Calcium	**30**
Iron	*****
Vitamin D	**25**
Vitamin B_6	**4**
Vitamin B_{12}	**15**
Phosphorus	**20**
Magnesium	**8**
Zinc	**4**
Pantothenic Acid	**6**

* Contains less than 2% of the nutrient.

The nutrient content of the eight-ounce glass of milk shown above closely approximates what would be found in Grade A milk that is pasteurized and homogenized and which has vitamin D added during processing. The information was obtained from the nutrition labels of milks produced in New York, California and Wisconsin. The U. S. Recommended Daily Allowance actually may vary slightly with different brands. Figures for the composition of whole milk are based on a fat content of 3.5 percent. FDA guidelines call for a minimum of 3.25 percent fat but such minimums vary in the different states with some milks above the minimums.

ated for up to six months. Once opened, it must be refrigerated. It has a slightly cooked flavor.

When a consumer buys grade A milk, the label usually says whether it is pasteurized or homogenized. Although it is mandatory to pasteurize grade A milk, FDA's regulations do not require that to be stated on the label. However, if it is ultra-pasteurized or homogenized, this must be stated on the label.

Homogenized milk has to be preheated first. When it is homogenized, it is forced through small openings under pressures of 500 to 2,500 pounds per square inch to reduce the size of the fat globules. This process equally disperses the fat globules throughout the milk and prevents separation of the cream from the milk; the net effect gives the milk a uniform consistency.

Milk enjoys a long-standing reputation as one of our more nutritious foods. In general, according to the United States Department of Agriculture, an eight-fluid-ounce serving of whole milk provides about 160 calories, approximately eight grams of protein, 12 grams of carbohydrate, nine grams of fat plus essential vitamins and minerals. (There are 28.35 grams to an ounce.) When the fat from milk is separated, as in skim and low-fat milks, the fat-soluble vitamins—A and D—and other fatty materials, such as cholesterol, are also removed.

Food and nutrition experts generally agree that the most noteworthy contributions of milk are protein, calcium and riboflavin. However, milk is not a good source of iron or vitamin C.

The protein in milk is of high quality because it contains the balance of essential amino acids required by the human body. The body needs protein to build and repair body tissues, form antibodies, hormones and enzymes and for other functions. The body's need technically is not for protein but for amino acids—the building blocks of protein. The major proteins in milk are casein and lactalbumin. The protein in milk contributes about 22 percent of the calories in whole milk.

Milk and other dairy products are major contributors of calcium to the human diet. Calcium is essential for the building of bones and teeth and for regulation of the central nervous system. Several years ago, a report by Colorado State University's food science and nutrition department noted that in the United States, Canada, the Netherlands and the Scandinavian countries, 75 percent or more of the daily intake of calcium came from milk and milk products.

Nutritionists have long been concerned about the decrease in dietary calcium because of a gradual decline in fluid milk consumption in this country. However, one saving grace has been the increased consumption of cheese and other dairy foods. Cheeses, yogurt and frozen desserts all provide generous amounts of calcium. For those concerned about limiting fat consumption, a glass of skim milk has as much calcium as whole milk and about half as many calories.

Riboflavin is a B vitamin that is plentiful in milk and other dairy products. It plays an important role in the body's chemistry and in its use of food for energy. Milk, meats, cheese, eggs and cereal products and some dark green vegetables are the chief sources of this vitamin. The National Dairy Council estimates that dairy foods contribute about 39 percent of the total riboflavin in the U.S. diet. Milk can lose riboflavin when exposed to light. Opaque containers and storage away from light help preserve the riboflavin.

Vitamin A plays an important role in maintaining skin, membranes and eyes so that they function properly and resist infectious agents. But it is a vitamin that is in short supply in the diets of some Americans. Vitamin A is naturally present in the fat protein of milk and milk products, but it is removed during processing when milk fat is separated from the milk. FDA regulations require its addition to low-fat and skim milk products.

Vitamin D plays an important role in enabling the body to absorb and use calcium and phosphorus to build strong bones and teeth. Earlier in the century, symptoms of rickets due to vitamin D deficiency were common among young children in this country. The addition of vitamin D to milk and some other foods, along with increased awareness of the need for this vitamin, has reduced rickets to the point where its symptoms are rarely seen today. Its addition to milk is optional under FDA regulations, but most milks sold do contain this vitamin.

Fat contributes about 48 percent of the calories in whole milk, or 77 calories in an eight-ounce serving. There are 10 grams of fat and 35 milligrams of cholesterol in that eight-ounce glass. However, a glass of skim milk has only a trace of fat and about four milligrams of cholesterol.

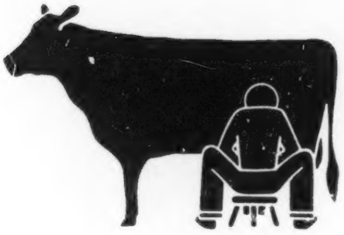
Lactose, or milk sugar, is the main carbohydrate in milk, and it contributes about 30 percent of the calories. Some people who drink milk and then suffer abdominal cramps, gas, bloating, diarrhea or other stomach distress often are found to have a deficiency of lactase, an enzyme essential to the digestion of lactose. The deficiency is found less often among

Federal Milk and Cream Standards

Product	Pasteurization	Ultra-Pasteurization	Homogenization	Fat % (min./range)	Non Fat Milk Solids % min.	Vitamin D	Vitamin A	Protein Fortified
Milk	M[a]	Opt.[b]	Opt.[c]	3.25	8.25	Opt.	Opt.	NP
Lowfat Milk	M[a]	Opt.[b]	Opt.[c]	0.5-2.0	8.25	Opt.	M	Opt.
Skim Milk [Nonfat Milk][e]	M[a]	Opt.[b]	Opt.[c]	<0.5	8.25	Opt.	M	Opt.
Half-and-Half	M[a]	Opt.[b]	Opt.[c]	10.5-18.0	NP	NP	NP	NP
Light Cream [Coffee Cream or Table Cream][e]	M[a]	Opt.[b]	Opt.[c]	18-30	NP	NP	NP	NP
Light Whipping Cream [Whipping Cream][e]	M[a]	Opt.[b]	Opt.[c]	30-36	NP	NP	NP	NP
Heavy Cream [Heavy Whipping Cream][e]	M[a]	Opt.[b]	Opt.[c]	36	NP	NP	NP	NP
Evaporated Milk	NP[d]	Opt.	M	7.5	25.5	M	Opt.	NP
Concentrated Milk [Condensed Milk][e]	M	Opt.	Opt.	7.5	25.5	Opt.	NP	NP
Sweetened Condensed Milk	M	Opt.	Opt.	8.5	28	NP	NP	NP
Nonfat Dry Milk	M	NA	NP	Max[f] 1.5	NA	NP	NP	NA
Nonfat Dry Milk Fortified with Vitamins A and D	M	NA	NP	Max[f] 1.5	NA	M	M	NA
Sour Cream [Cultured Sour Cream][e]	M	Opt.	NP	18	NP	NP	NP	NP
Acidified Sour Cream	M	Opt.	NP	18	NP	NP	NP	NP
Sour Half-and-Half [Cultured Half-and-Half][e]	M	Opt.	NP	10.5[g]-18.0	NP	NP	NP	NP
Acidified Sour Half-and-Half	M	Opt.	NP	10.5[g]-18.0	NP	NP	NP	NP

Opt. —use of process/ingredient is *optional*
M —use of process/ingredient is *mandatory*
NP —no provisions specified in standards
NA —not applicable
a Pasteurization is mandatory but declaration of term PASTEURIZED is *optional*
b "Ultra-pasteurization" is an optional process—declaration of term ULTRA-PASTEURIZED is mandatory on principal display panel, if applicable
c For *all* products Homogenization *and* label declaration (Homogenized) are both optional
d It is, however, so processed by heat, either before or after sealing of the container, so as to prevent spoilage.
e Name(s) in [brackets] are acceptable alternate product names
f Maximum % milkfat
g Not less than 8.4% when combined with bulky flavoring ingredients

Adapted from National Dairy Council table.



Caucasian than among non-Caucasian people.

It should be emphasized, however, that the problem is something that can only be confirmed by medical diagnosis. A person with lactase deficiency is not likely to have complete intolerance to lactose and some people can drink moderate amounts of milk. A physician's advice is needed to help determine the degree of restriction necessary for milk and other lactose-containing products. Fermented milk products in which some lactose is converted to other chemical substances may be tolerated better than non-fermented milk products, as will yogurt, aged cheeses and cottage cheese. Lactase enzyme preparations, which may be added to milk to convert the lactose to other sugars, also are available. The preparations tend to give milk a sweeter flavor.

When milk gets to the marketplace, it comes in many varieties. Whole milk must consist of at least 3.25 percent milk fat and at least 8.25 percent non-fat milk solids. Low-fat milk has at least 8.25 percent non-fat milk solids, but milk fat is removed so that its content ranges from 0.5 percent to 2.0 percent. Skim milk has 0.5 percent fat or less. Both low-fat and skim must be pasteurized or ultra-pasteurized and also may be sold as a homogenized product. For both kinds, the addition of at least 2,000 international units of vitamin A to each quart is mandatory, but the addition of vitamin D to low-fat milk is optional. Both milks may be fortified with non-fat milk solids to increase the levels of protein.

The labels must identify skim or low-fat milk and must state the percentage of milk fat. In addition, the labels must declare the addition of vitamin A and, when added, vitamin D as well. When non-fat milk solids are added at a level of 10 percent or more, the label then must say it is "protein fortified" or "fortified with protein."

Chocolate milk—low-fat and skim milk varieties also are available—are flavored with chocolate syrup or cocoa powder. The chocolate solids concentration ranges from 1 percent to 1.5 percent. A nutritive sweetener, usually sucrose, comprises about 5 percent to 7 percent of the product, but its caloric value varies according to the milk fat content and other ingredients that are added, the Dairy Council reports. The milks are pasteurized and are usually homogenized and fortified with vitamins A and D.

Evaporated milk is preheated so that about 60 percent of the water is removed. FDA's standards require a milk fat content of 7.5 percent and a milk solids content of at least 25 percent. Each fluid ounce must contain at least 25 international units of vitamin D and the product must be homogenized and also sealed in a container and processed by heat, either before or after sealing, to prevent spoilage. Evaporated milk can be stored without refrigeration until opened. Once opened, the milk should be transferred to a clean, opaque container and refrigerated. FDA regulations say evaporated skim milk must consist of at least 20 percent milk solids and not more than 0.5 percent milk fat unless otherwise indicated. Each fluid ounce must have 125 international units of vitamin A and 25 units of vitamin D.

Condensed or concentrated milk is produced mainly for dairy industry use. The milk fat and solids content is the same as that for evaporated milk. Sweetened condensed milk, according to FDA regulations, is obtained by partial removal of "the water only from a mixture of milk and safe and suitable nutritive carbohydrate sweeteners." In packaged form, it must consist of at least 8 percent milk fat and at least 28 percent milk solids. The amount of nutritive sweetener added must be sufficient to prevent spoilage. Sold in small cans, the milk contains about 60 percent water and 40 percent to 45 percent sweetener, usually sucrose, which acts as a preservative.

Non-fat dry milk is made by removing water from pasteurized skim milk. Its moisture content must be no more than 5 percent of its weight and not less than 1.5 percent milk fat, according to FDA's standards. Almost all instant non-fat dry milk sold at retail is also fortified with vitamins A and D. Instant non-fat dry milk mixes easily in cold water.

Dry whole milk is pasteurized milk with the water removed. It contains lactose, protein, fat and minerals in the same relative amounts as the milk from which it is made. Its milk fat content, says FDA, can range from 26 percent to 40 percent. The product is susceptible to oxidation, but this is minimized by packaging the dry whole milk in gas and vacuum pack containers impermeable to air.

Low-sodium milk, though not readily available, is produced for consumers on sodium-restricted diets. About 95 percent or more of the sodium that occurs naturally in milk can be removed by ion exchange. With this process the sodium content of eight fluid ounces of whole milk can be reduced from the normal level of about 120 milligrams to about six milligrams. When subjected to an ion-exchange resin process, the sodium is replaced by potassium. These milks are pasteurized and homogenized.

Chris Lecos is a member of FDA's public affairs staff.

You see your doctor, get a prescription, have it filled and take the medicine. Isn't that all you need to know about prescription drugs?

No!

Drugs are powerful chemicals. Along with their benefits, they also have a potential for harm.

Everyman's (Woman's, Too) Guide To Rx Drugs

Adverse Reactions

Some drugs can cause side effects (adverse reactions). Usually these are mild—a slight rash, mild headache, nausea or drowsiness; sometimes they are severe—prolonged vomiting, bleeding, marked weakness or impaired vision or hearing.

These are warning signals that the drug is causing problems. When a reaction is unexpected or severe a doctor should be consulted immediately.

Not everyone reacts the same way to medication. One person may experience a reaction to a certain drug, while another person may have no problems at all.

Drug-Drug Interactions

Two or more drugs, taken at the same time, can interact and affect the way one or the other behaves in the body. For example, an antacid will cause a blood-thinning (anticoagulant) drug to be absorbed too slowly, while aspirin greatly increases the blood-thinning effect of such drugs.

Two drugs with the same effect when taken together can sometimes have an impact greater than would be expected. This is called potentiation. Potentiation can be helpful, as when the antibiotic trimethoprim is used to boost the effect of another antibiotic, sulfamethoxazole, in combatting certain infections.

Potentiation also can be dangerous, particularly when several central nervous system depressing drugs are involved. Even non-prescription drugs, such as antihistamines that are often used to fight colds, can increase the sedative effects of anesthetics, barbiturates, tranquilizers and some pain-killers.

Food and Drug Interactions

Food can interact with drugs, making them work faster or slower or even preventing them from working at all. Here are some examples:

Fatty foods, eaten before the anti-fungal drug griseofulvin is taken, can cause blood levels of the drug to rise markedly. Calcium in dairy products impairs absorption of tetracycline, a widely used antibiotic. Citrus fruits or juices containing ascorbic acid speeds the absorption of iron from iron supplements. Soda pop, fruit and vegetable juices with high acid contents (such as grape, apple, orange or tomato) cause some drugs to dissolve in the stomach instead of the intestines where they can be more readily absorbed.

Large amounts of liver and leafy vegetables may hinder the effectiveness of anti-coagulants because vitamin K in these foods promotes blood clotting. Soybeans, rutabagas, brussels sprouts, turnips, cabbage and kale contain a substance that inhibits production of thyroid hormone; thus they can interfere with thyroid medications.

The most hazardous food-drug interaction is that of drugs sometimes prescribed for severe depression or high blood pressure and foods containing the substance tyramine. The drugs involved contain monoamine oxidase (MAO) inhibitors. The foods involved include aged cheese, Chianti wine, pickled herring, fermented sausages, yogurt, sour cream, chicken liver, broad beans, canned figs, bananas, avocados and foods prepared with tenderizers. Mixing these foods with an MAO inhibitor drug can raise the blood pressure to dangerous levels.

The food-drug interaction can go the other way. Oral contraceptives, for instance, are known to lower blood levels of folic acid, a member of the vitamin B family, and vitamin B_6 although the depletion is usually not serious enough to cause symptoms. Women who take birth control pills would be wise to include dark green leafy vegetables in their diet.

Chronic use of antacids containing aluminum can cause phosphate depletion, leading to weakness, malaise and loss of appetite.

Drugs and Alcohol

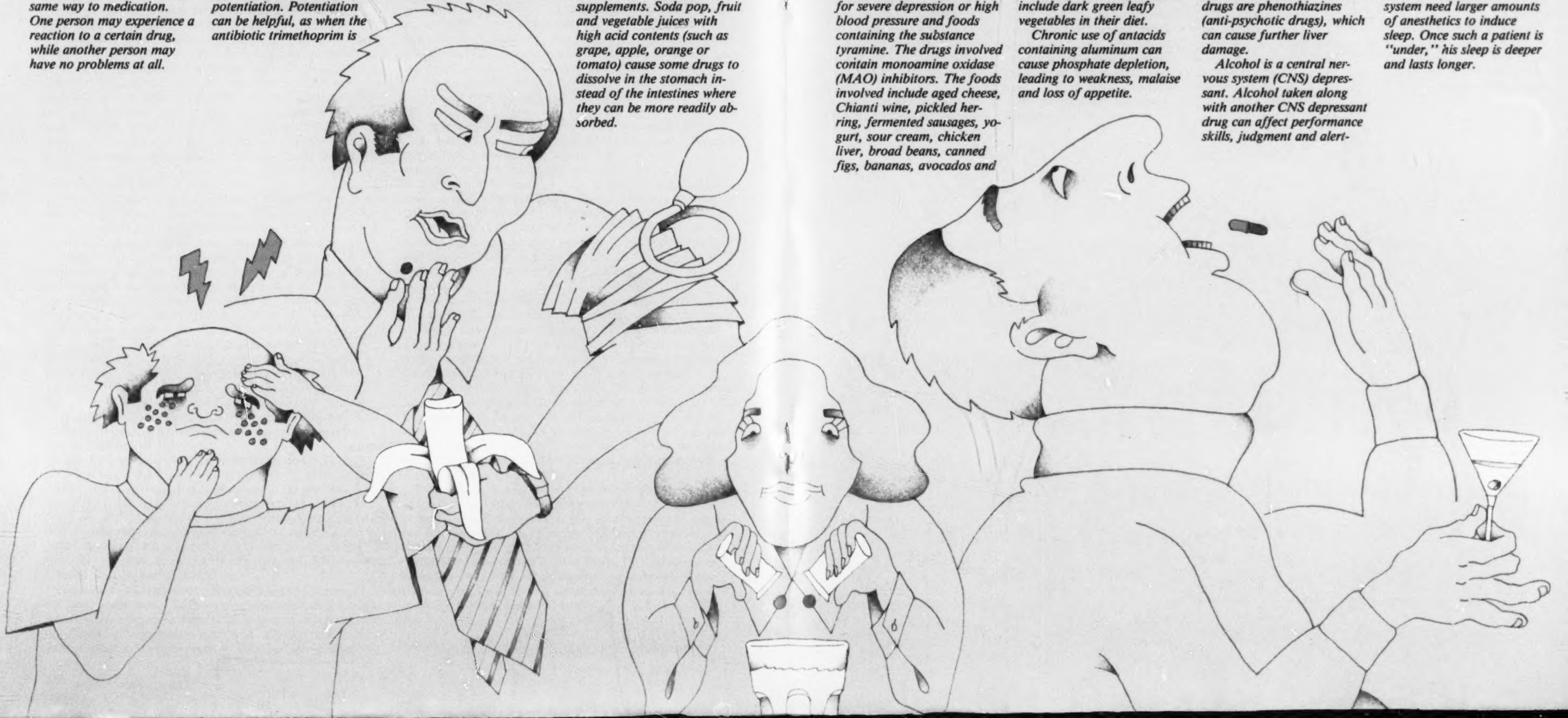
Chronic use of alcohol can cause changes in the liver that speed up the metabolism of some drugs, such as anticonvulsants, anti-coagulants and diabetes drugs. They become less effective because they do not stay in the body long enough.

Prolonged alcohol abuse can also damage the liver so that it is less able to metabolize or process certain drugs. In that case, the drugs stay in the system too long. This is particularly serious when the drugs are phenothiazines (anti-psychotic drugs), which can cause further liver damage.

Alcohol is a central nervous system (CNS) depressant. Alcohol taken along with another CNS depressant drug can affect performance skills, judgment and alertness. If the mixture includes overdoses of barbiturates, diazepam (Valium) or propoxyphene (Darvon), the result can be fatal.

A person who has developed a tolerance to the sedative effects of alcohol may need larger doses of tranquilizers or sleeping pills to get the desired effect. This can lead to an overdose without the person being aware of it.

Similarly, alcoholics and patients with alcohol in their system need larger amounts of anesthetics to induce sleep. Once such a patient is "under," his sleep is deeper and lasts longer.



Drugs and Smoking

Women on birth control pills who smoke have an increased risk of heart attack, stroke and other circulatory diseases.

Nicotine and other tobacco constituents speed up the metabolism of theophylline, an asthma drug, and pentazocine, a pain-killer, and to a lesser extent certain tranquilizers, analgesics and antidepressants. Thus, smokers may need larger than normal doses of these drugs. When they stop smoking, dosage of these drugs may have to be changed.

Smoking also can affect certain diagnostic tests, such as red and white blood cell counts and blood clotting time determinations.

Drugs and Laboratory Tests

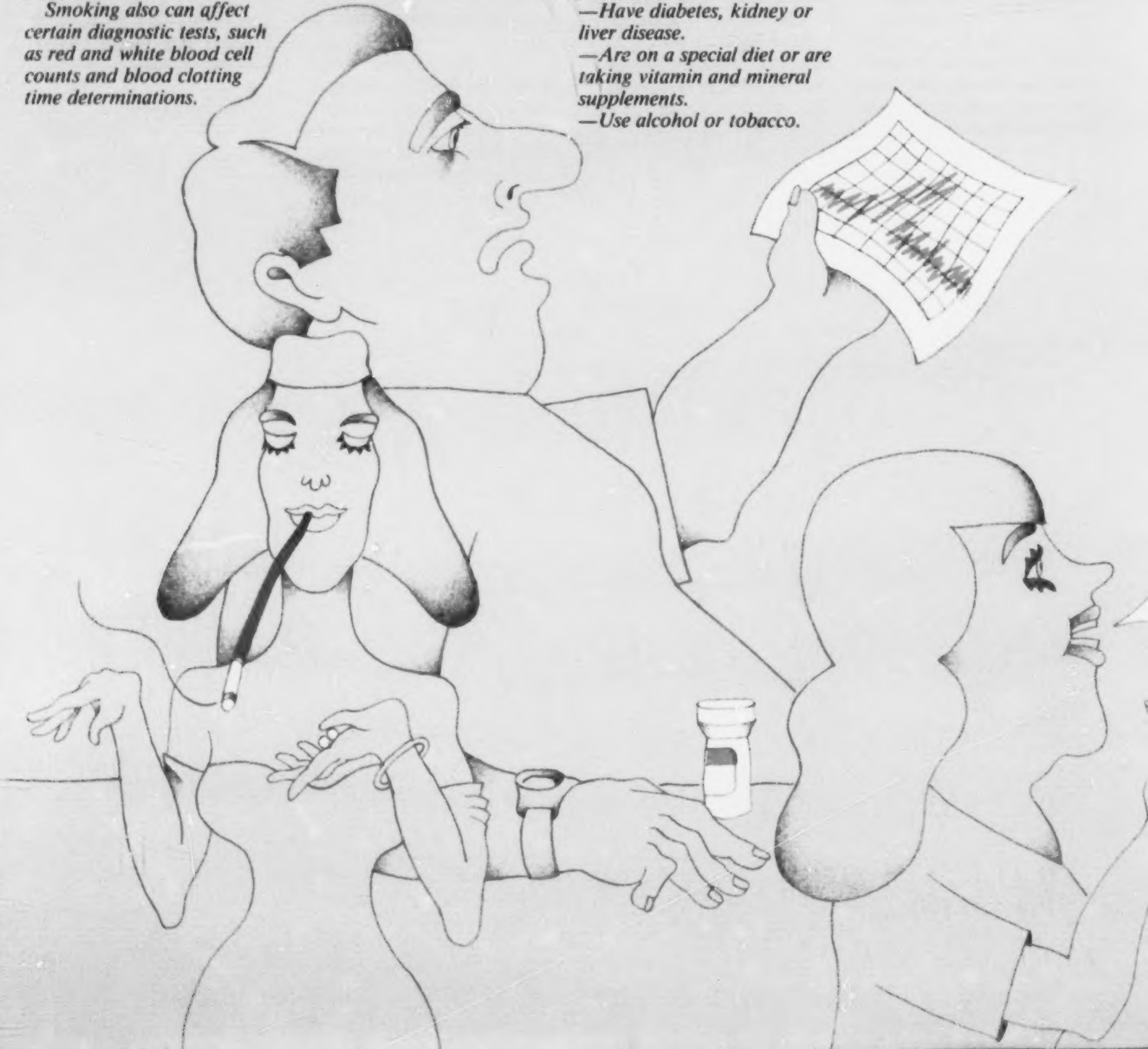
Drugs can affect the results of clinical laboratory tests. For example, excess use of laxatives can affect tests to determine calcium or bone metabolism. Penicillin can result in false readings of protein in the urine, a sign of kidney disease. Large doses of vitamin C can produce false results in a urinary glucose test for diabetes.

What You Should Tell Your Doctor

Because of these side effects and drug interactions, it is important that you tell your doctor if you:
—Have had allergic reactions to drugs or foods, such as rashes or headaches.
—Are taking any medications on a regular basis, such as contraceptives or insulin, or if you use any non-prescription drugs on a routine basis.
—Are being treated for a different condition by another doctor.
—Are pregnant or breastfeeding.
—Have diabetes, kidney or liver disease.
—Are on a special diet or are taking vitamin and mineral supplements.
—Use alcohol or tobacco.

What You Should Ask Your Doctor

To get the most out of your medicine, you should ask your doctor:
—What is the name of the medicine? Write it down so you won't forget.
—What is the medicine supposed to do? (Make the pain go away? Get to the cause of the pain? Reduce fever? Lower blood pressure? Cure infection?)
—What side effects might occur?



—How should you take the medicine? Does "three times a day" mean morning, noon and night? Should you take it before meals, with meals, or after meals? If the directions say "every six hours" do you have to get up during the night to take the medicine on time?

—How long should you take the medicine? If you stop just because you feel good, the symptoms and the disease may recur.

—Are there other medicines you should not take while you are taking this one?

—Are there any foods or beverages you should avoid?

—Should you avoid alcoholic beverages while taking the drug?

—Can the prescription be refilled without an appointment or does the doctor need to see you again?

What's on Your Prescription

The first word on the prescription is the name of the drug. Next is the dosage form (liquid, capsules, tablets) and the strength (such as 250 mg, or milligrams). Next is the amount you will get (15 capsules, 5 fluid ounces), followed by the directions for use. These are often abbreviations of Latin words. For instance, ter in die, *written t.i.d., means three times a day. The pharmacist will translate this information on the label of the medicine container. The prescription form will also indicate how many times the prescription can be refilled.*

It's a good idea to check the prescription before you leave the doctor's office. If there is anything you don't understand, ask about it.

Information for Patients

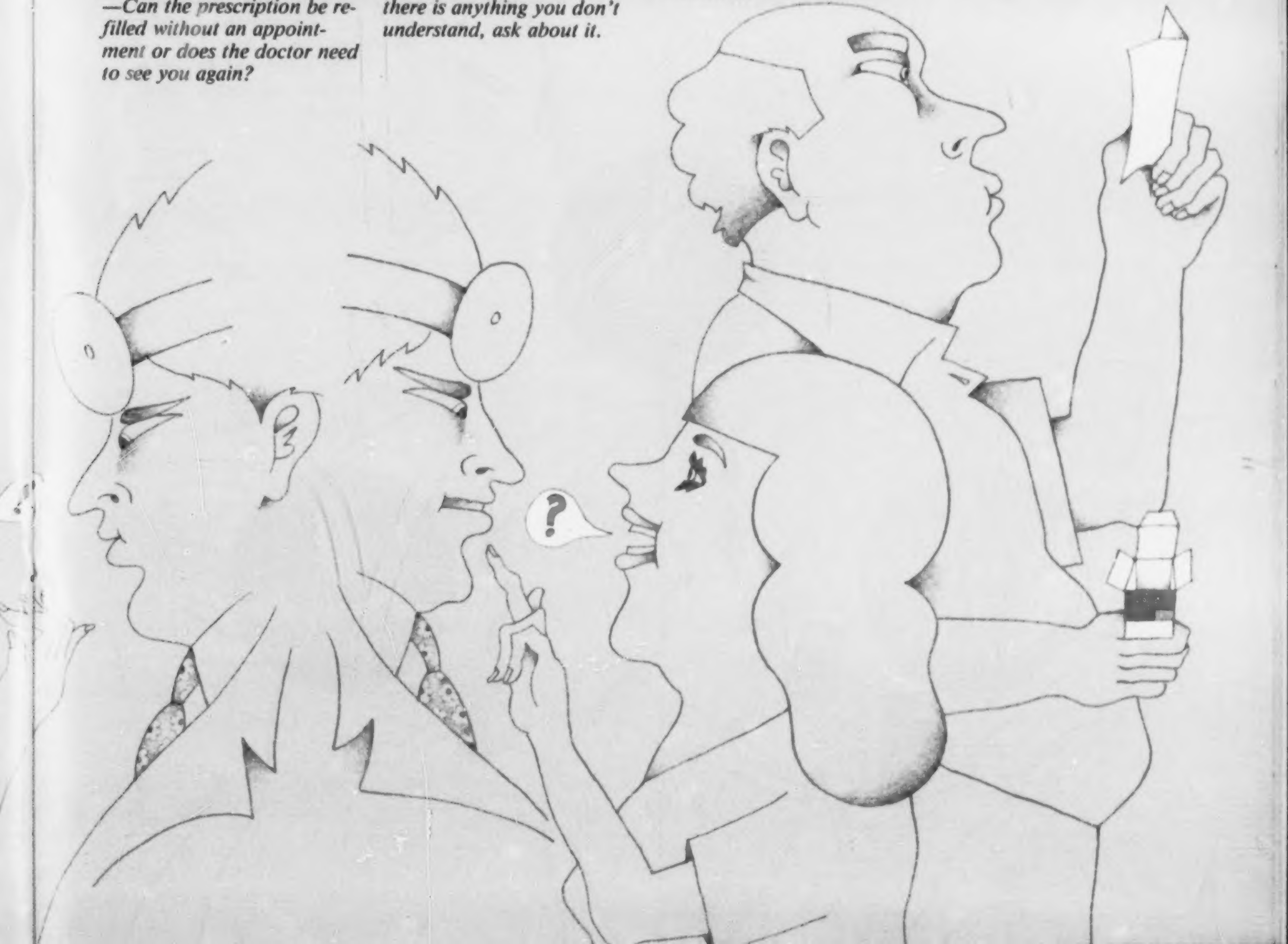
Detailed information for patients does not have to accompany most prescription drugs. But for a few, such as contraceptives and estrogens, the Food and Drug Administration does require a leaflet or brochure that tells about the benefits and risks of these products. If there is such a brochure with a drug prescribed for you, be sure to read it carefully and if you have questions, ask your doctor or pharmacist.

Non-prescription drugs must include on their labels information about when and how to take the product, possible side effects or drug interactions. Always read these labels before taking the medicine.

Drug Costs: Brand vs. Generic

When a new drug is discovered it is patented and given a brand, or trade, name. The drug company has exclusive rights to that product for 17 years. When the patent expires, other companies may manufacture that drug under another brand name or under the drug's generic, or common, name. These drugs often are less expensive than the original drug.

Almost all states now permit pharmacists to dispense a generic drug instead of a



brand name product if the doctor approves. However, not all drugs are available from more than one company, and not all multisource drugs are "therapeutically equivalent"—that is, behave in the same way in the body.

FDA publishes lists of drugs that identify which ones can be substituted safely. The next time your doctor writes you a prescription, ask if there is an approved generic version of the drug.

Here are some tips to help you use prescription drugs safely and effectively:

—If a drug is not doing what it is supposed to do for you, check with your doctor. You may need a different dosage or a different drug.

—If you have an unexpected symptom—rash, nausea, dizziness, headache—report it to your doctor immediately.

—Don't stop taking your medicine just because you're feeling better. You may prevent the drug from doing its work completely.

—Check drug labels for specific instructions or warnings, such as "do not take on an empty stomach" or "do not take with milk."

—Check the label, or ask the pharmacist, for storing instructions. Some drugs should be refrigerated; others must be protected from light.

—Always keep medicines out of the reach of children. Even though most prescription medicines come in childproof containers, children sometimes can open these bottles and swallow the contents. (If you have difficulty opening such safety closures, you can request bottles with regular caps.)

—Never let another person use your medicine and never take medicine prescribed for anyone else. Your symptoms may look the same, but you may be suffering from an entirely different problem.

—Never take medicines without checking the label to make sure you're taking the right one. Don't take medicine at night without turning on the light.

—Don't transfer medicines from the original container. These containers are designed to protect the drugs. Fancy pill boxes are not always suitable.

—Do not keep prescription drugs that are no longer needed. Destroy leftover medicines by flushing them down the toilet and dispose of containers carefully so children can't get them.

—Keep a list of all drugs you are taking to show to your doctor and your pharmacist.

—If you are taking several different drugs and have trouble remembering when and how to take them, your pharmacist may be able to provide you with a handy checklist.

GENERIC
NAME BRAND

Hypertension Targets: Blacks, Elderly

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Hypertension Targets: Blacks, Elderly

by Roger W. Miller

There's no telling who will develop high blood pressure. But some people are more likely candidates than others: blacks, for example, and the elderly. Also, those with a family history of elevated blood pressure readings are likely to develop the same.

Among adults 25 to 74, according to the National Health Survey done by the National Center for Health Statistics, the high blood pressure rate among blacks is 48.8 percent. For persons aged 65 to 74, some 47.6 percent (including 55 percent of the blacks) have high blood pressure, or hypertension as it is also known.

That hypertension is apt to run in the family is well documented. Researchers have detected elevated blood pressure readings in youngsters from families with a history of such readings.

Researchers have also bred hypertension into some strains of rats and other animals in just two generations, using high-salt diets to induce and maintain the high readings.

Hypertension is associated with heart attack, stroke and kidney disease. Stroke and coronary heart disease are the nation's major killers, although the death rates for the diseases have been declining—in large measure because of better detection means. From 1968 through 1978, the stroke death rate in the United States dropped by 36.5 percent, while heart attack deaths went down 25.1 percent.

For non-white males, however, the death rates from stroke remain well above those of white males. In 1978 (the last year for which figures are available), deaths among white males from stroke were 46.8 per 100,000. But for non-white men, the rate was 76.5. The ratios were much the same for white and non-white females.

The coronary heart disease death rate for non-white men in 1978 was slightly lower than for white men, but more non-white women died from the disease than their white counterparts.

The body's diminished fine tuning is the reason for higher blood pressure among the elderly, but accounting for elevated readings among the black population in this country is not so simple.

The disease usually hits blacks sooner and harder. The hypertension rate for blacks aged 25 to 34 is 19.1 percent compared to 8.1 percent for whites. That 2-to-1 ratio remains into the 50s. Before age 50, death rates from hypertension and hypertensive heart diseases have been 6 to 15 times higher among blacks than whites.

Some early research in this country had indicated that skin pigmentation and high blood pressure are related—that is, the darker the skin the higher the blood pressure. But that theory has largely been discredited and would not account for those areas of the world where dark-skinned populations do not automatically show high blood pressure readings.

There is some argument that the social and economic position of blacks in the United States may contribute to their tendency to develop high blood pressure. This argument is based on the belief that stress contributes to hypertension.

One researcher who backs this theory is Dr. Richard F. Gillum of the University of Minnesota School of Medicine. Writing in *Hypertension*, the magazine of the American Heart Association, Gillum said: "Blacks are more frequently exposed to conditions of poverty, low occupational and education status and high levels of socioecologic stress, all of which are related to the prevalence of hypertension in both blacks and whites."

Much evidence points to salt or sodium as a main reason for so many American blacks having to do battle with high blood pressure. Surprisingly, it may not be that blacks eat too much salt, but it's what their bodies do with the salt they eat.

Tracing the roots of black Americans tells much. Most black Americans are descended from Africans who lived in the west central part of that continent, a climate or area that may have taught the body to conserve on salt. Arthur Grollman of the University of Texas Southwestern Medical School wrote in the *Texas Report on Biology and Medicine:*

"Sodium is not always available in the environment in sufficient amounts for supplying the needs of the organism. A deficiency of this vital element is apt to exist in areas distant from the sea, in hot climates and, particularly, in individuals restricted to a potassium-rich vegetable diet."

The potassium in the diet is significant. Researchers say that potassium plays an important role in the prevention of hypertension. The balance between sodium and potassium is delicate and intertwined.

Just as the sickle cell may have developed in blacks as a protection against malaria, so the ancestors of American blacks may have developed a system that tends to retain salt. Indeed, numerous studies show that blacks excrete less sodium in their urine (which is where the body dumps excess sodium) than whites. It seems that the body was simply making more efficient use of a scarce item.

But the blacks were thrown into the milder U.S. climate where perspiring was not a year-round necessity, and they were thrown into a society that loved salt. The result probably adds up to today's high blood pressure problems among black Americans.

Researcher Gillum puts it this way:

"Investigators reporting these data hypothesize that blacks may have evolved more efficient mechanisms for renal (kidney) sodium conservation to cope with the low sodium intake in tropical or subtropical environments and that this protective mechanism may place blacks at a disadvantage when exposed to high sodium intake of western diets, resulting in greater propensity to hypertension."

As to the somewhat popular notion that blacks may eat too much salt, particularly in "soul" food, the evidence isn't there. Said Gillum: ". . . there is no objective documentation of higher sodium intakes in blacks than in whites despite many anecdotal observations to the contrary."

In other words, don't believe all those stories you've heard about blacks using too much salt. Gillum's remark notes the lack of evidence. Few studies have been done. One often cited, in Evans County, Ga., didn't show that much difference between white and black salt consumption.

In its "Final Report on High Blood Pressure Education and Control," the National Black Health Providers Task Force had a series of recommendations regarding sodium, blacks and hypertension. The recommendations ranged from using sodium restriction as "definitive therapy," to more research into such areas as eating habits, to development of a cookbook for black hypertensives.

The task force's report, issued this spring, resulted in the formation of a Trilateral High Blood Pressure Control Project that will combine the efforts of the American Red Cross and black public, private and voluntary groups to work on the problem of high blood pressure among blacks.

The Food and Drug Administration, which has been waging a campaign to make the public aware of the health consequences of excess sodium consumption, is working with the trilateral group. FDA plans to target specific high blood pressure education programs at blacks and the elderly.

Roger W. Miller is editor of FDA Consumer.

Consumer Forum

No Color in Catsup

This is regarding your article "The Tanning Pill, A Questionable Inside Dye Job" by Louise Fenner, which appeared in your February 1982 issue of *FDA Consumer*. On page 25, the statement "Both carotene and canthaxanthin are approved by FDA as color additives in foods . . . catsup . . ." is in error. The FDA standard of identity for catsup, *21 CFR* Part 155.194, does not permit the addition of color to this product, in any form.

Howard R. Lacey
Technical Director
Brooks Foods
Mount Summit, Ind.

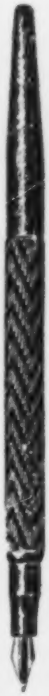
Mr. Lacey is correct. The standard of identity for catsup does not permit the addition of color in any form. Therefore, neither beta carotene nor canthaxanthin may be added to standardized catsup. However, imitation catsup, which does not comply with the standard of identity, may contain the added colorings as long as it is properly labeled.

Sugar Use at Issue

The heading of the update "Sugar Consumption Declines" (*FDA Consumer*, Feb. 1982) is highly misleading. It should have read "Sugar Consumption Continues to Climb." While per capita consumption of sucrose (from cane and beet) totaled 79.7 pounds last year (not "about 75 pounds" quoted), the great increase in the use of corn sweeteners pushed the annual average consumption of all caloric sweeteners to a total of 125.9 pounds (USDA's *Sugar and Sweetener Outlook & Situation*, Feb. 1982, p. 28).

Even this total is misleading. Sugars found as natural constituents in foods need to be considered as another factor in the total sugar consumption. According to the National Institute of Dental Research, the average American eats about 165 pounds of sugar a year. ("Snack Facts," Pub. 81-1680, NIH, Sept. 1981).

Elsewhere in the same issue of *FDA Consumer*, Feb. 1982, a writer stated " . . . for healthy people who can maintain normal weight, eating lots of sweets hasn't been found detrimental except possibly in causing tooth decay." This statement ignores a mounting body of evidence from professionals in various disciplines that appears to incriminate high sugar consumption with a wide variety of health problems, in addition to tooth decay. This statement also runs counter to the recommendation, given to the public repeatedly, by agencies such as Health and Human Services, National Institutes of Health, and others, to reduce sugar consumption.



Beatrice Trum Hunter
Hillsboro, N.H.

Headlines are necessarily terse. The article covers both the drop in refined sugar consumption and the increase in use of sweeteners produced from corn. A headline covering both aspects of the story would have been unwieldy and simply would not have fit in the space available. Thus, we chose to highlight information in the first paragraph. Since most people think of the refined product when they hear the word "sugar," we don't believe the headline was misleading.

Incidentally, we rounded the 1981 per capita sugar consumption figure to "almost 80" pounds. The 75-pound figure represented consumption in 1946.

As to the contribution, or lack of it, that sugars provide to the diet, FDA sticks by the statement cited in the February issue.

Herpes Article Questioned

Your November 1981 article, "Herpes Thrives on the Sexual Revolution," is an insensitive and misleading look at a very important issue. It is obvious that Ms. Fenner did not do her homework when she prepared this report whose title is more fitting for a grocery store tabloid than the *FDA Consumer*.

Contrary to what Ms. Fenner may think, thousands of herpes sufferers, including myself, are not members of the "sexual revolution." Herpes thrives, all right. It thrives on misinformation and an uneducated public. Herpes doesn't care if you are black or white, man or woman, or a member of the "sexual revolution." It can infect anyone unfortunate enough to be exposed.

Ms. Fenner did have the good sense to consult an excellent source, Dr. Richard Hamilton's *The Herpes Book*, which she quoted but apparently failed to read. She states that "unlike the others (syphilis and gonorrhea), herpes cannot be cured or even effectively treated." Elsewhere she says that "because there is no effective therapy for herpes, prevention is extremely important." Dr. Hamilton points out, as do others in the field, that herpes victims under emotional and physical stress suffer more severe and frequent outbreaks. One of the most useful forms of therapy is not to allow oneself to become tired or run down. The relationship between emotional stress, or one's mood, and our bodies' immune system is just beginning to be explored. But even at this early stage, the link between emotional stress and herpes outbreaks is realized. So, paying close attention to one's physical and emotional well being is indeed universally recognized as a most important form of therapy.

Being a publication whose job it is to disseminate information regarding drugs, I found Ms. Fenner's report, again, lacking. As well as her brief reference to interferon I would like to have seen reference made to acyclovir (ACV). ACV's promising results (*New England Journal of Medicine*, 1981, 305:63-7) have stirred up quite a clamor in the popular press. I was also disappointed that there was no discussion of 2-deoxy-D-glucose, isoprinosine, ribavirin, L-lysine and others.

Furthermore, Ms. Fenner's statement that " . . . herpes simplex infection is usually no more than a big annoyance to an adult . . . " shows her lack of understanding and sensitivity to the enormous emotional issues involved with this disease.

A fair representation of all the facts would have given the reader help and possibly some hope. But perhaps Ms. Fenner believes that members of the "sexual revolution" are too busy being promiscuous to read.

James W. Honeycutt
Portland, Ore.

We regret that the article on genital herpes seemed insensitive to Mr. Honeycutt. The purpose in writing it was to inform readers about a sexually transmitted disease that is claiming up to half a million new victims each year.

We are, of course, aware of acyclovir, 2-deoxy-D-glucose, and other therapies being tried against herpes. On March 30, 1982, FDA announced the approval of acyclovir ointment to help manage genital herpes. It is the first drug to be approved for this purpose (see Updates, page 3). Others are still in various experimental stages.

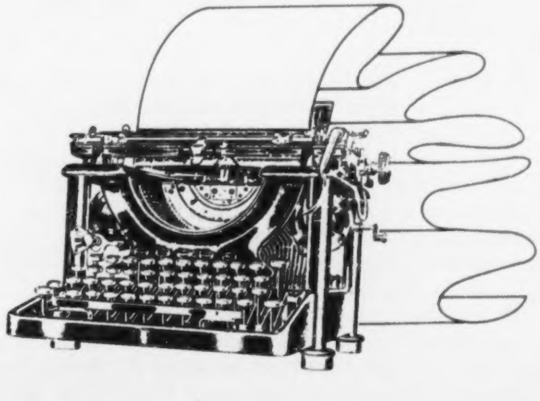
The article does mention the connection between stress and the recurrence of genital or labial herpes outbreaks. As Mr. Honeycutt himself points out, the relationship between stress, the body's immune system and disease is just beginning to be explored. Although avoiding stress and maintaining good health may reduce recurrences for some herpes patients, scientific evidence does not exist to support a claim that this regimen is "an important form of therapy." Given so many unknowns about the disease, well-controlled studies are needed to support claims for any form of therapy.

In stating that herpes "thrives on the sexual revolution," we were simply noting that the chances of exposure to and contraction of herpes (and certain other diseases) have increased as a result of the sexual freedom that exists now in our culture. The U.S. Centers for Disease Control reported on March 26 of this year that genital *herpes infections appeared to occur at epidemic proportions between 1966 and 1979—the last year for which figures are available.*

The statement that herpes "is usually no more than a big annoyance to an adult" was intended to highlight the difference between its physical effects in most adults and its potentially devastating effects in newborns (death or permanent visual or neurological impairment).

Individuals with further questions about herpes may wish to call the National VD Hotline at (800) 227-8922 or write to:

Herpes Resource Center
P.O. Box 100
Palo Alto, Calif. 94302



The Notebook: a potpourri of items gathered from FDA press releases, the Federal Register *and other news sources. The* Federal Register *(designated FR with date of publication) is available in many large public libraries.*

■ **Correction:** The caption of page 9 of the March 1982 issue of *FDA Consumer* incorrectly identified the contents of Searle's Nitrodisc as "nitrogen." The drug in the disc is nitroglycerin, used to treat angina.

■ The changing scene at FDA: **Dr. Harry M. Meyer Jr.** has been appointed director of the Bureau of Drugs, succeeding Dr. Richard Crout who has held that post since 1973. Meyer has headed the Bureau of Biologics the past 10 years . . . . **Dr. Marion Finkel,** formerly associate director for new drug evaluation, has been named director of orphan drug products in the Office of the Commissioner.

■ **Rubber nipples** used on infant feeding bottles contain nitrosamines, FDA has told the members of the Rubber Manufacturers Association and the Infant Formula Council. Although the amount of nitrosamines ingested by infants from the nipples is extremely small (less than 1 part per million) and there is no evidence that acute or chronic health effects have resulted, the occurrence of nitrosamines in rubber nipples is of concern. FDA has asked the two groups to share any scientific data on the problem and has asked manufacturers to investigate possible changes in manufacturing processes aimed at either eliminating or substantially reducing formation of nitrosamines.

■ The Department of Health and Human Services will support legislation to **extend patent protection** for products by the amount of time spent on government safety testing. Also backed is a proposal that would extend "process" patents to encourage development of new ways to produce existing products. New processes include biosynthetic production of human insulin, human interferon and human growth hormone.

■ Effective April 1 the Bureau of Biologics became responsible for regulating medical devices that are also licensed **biological products** or used in the production of licensed biologicals. The Bureau of Radiological Health has assumed greater responsibility for regulating **radiation-emitting devices.** The Bureau of Medical Devices will continue to develop major medical device policies and be responsible for manufacturer registration and device listing. The biologics and radiological health bureaus will process pre-market notifications, pre-market approval applications and investigational device exemption applications (FR April 9).

■ FDA is permanently listing **D&C Green No. 6** for use in externally applied drugs and cosmetics (FR April 2). Final reports have been received on 14 of 23 other color additives for which FDA requires additional safety tests. The 23 color additives are still on the agency's "provisional" list, permitting their use until a determination is made of their safety.

■ NOTES FROM THE MARKET BASKET: The Select Committee of the Federation of American Societies for Experimental Biology said there is no health hazard from **activated carbon** at present levels of use in foods to remove impurities that cause undesirable color, taste or odor in liquid products or in processing water. The committee also found there is no health hazard from smoke flavoring solutions, including smoked yeast flavoring. Smoke flavoring solutions are condensates of smoke produced by the burning of hardwood in a limited amount of air. They are used as a flavor for various foods, mainly meats, and as an anti-oxidant to retard bacterial growth. . . . FDA is no longer considering **establishing a U.S. standard** for canned tropical fruit, quick frozen blueberries, quick frozen leeks, powdered dextrose or powdered sugar based on recommended international (Codex) standards because there is no interest in or need for such standards (FR March 26 and April 9). . . . **Labels** on diluted fruit and vegetable beverages won't have to show the percent of each juice in the product until July 1, 1984. The compliance date was moved up two years to allow FDA to study this rule along with two similar regulations now under review concerning diluted orange juice and non-carbonated beverages (FR March 26) . . . . FDA and the Royal Norwegian Ministry of Agriculture have signed an agreement, effective Feb. 26, under which the Norwegian ministry will assure that contaminated or underprocessed **rennet casein,** a milk byproduct, will not be exported to the United States. This will minimize the need for extensive FDA audit sampling (FR April 9).

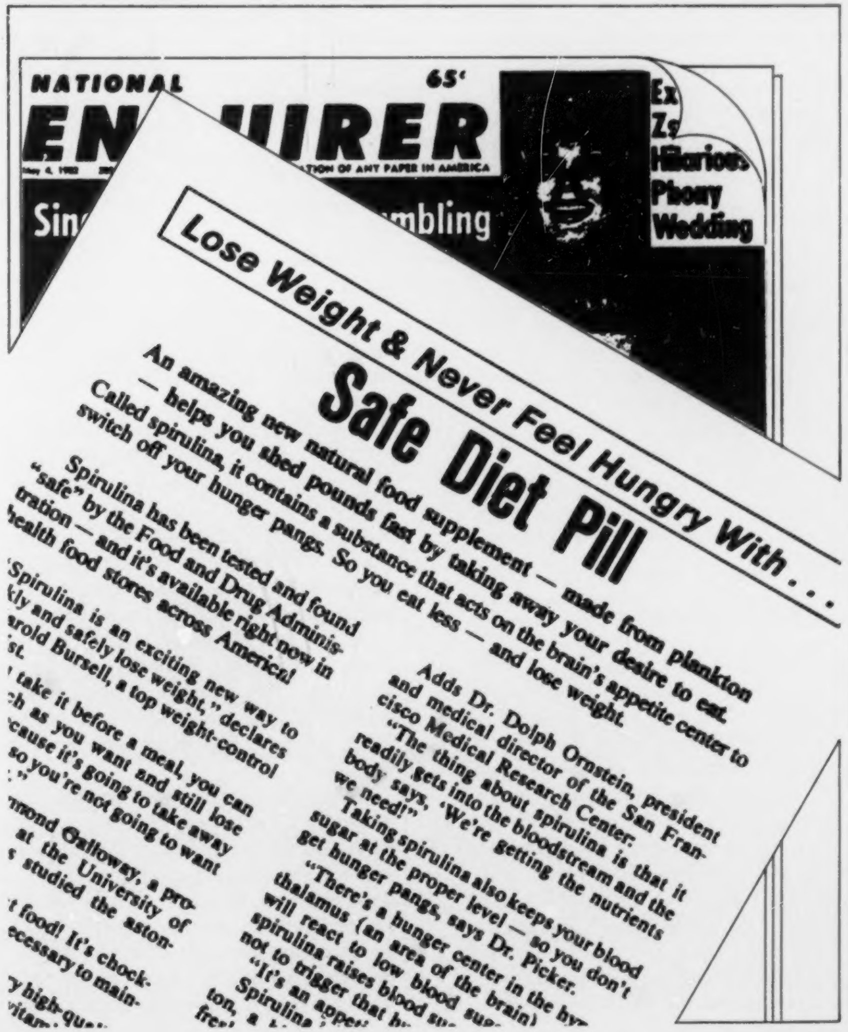
Spirulina, A Miracle Food It's Not

by Carol Ballentine

Spirulina. It could be a pop song, a breakfast cereal, even a strip-tease artist. But it's really a blue-green alga that has become a best seller in health food stores. Recently, Microalgae International Sales Corp. (MISCORP), a firm in Santa Cruz, Calif., paid a $225,000 penalty for making false claims about spirulina.

MISCORP isn't the only firm that has been making inflated claims about the alga. Others jumped on the bandwagon in the summer of 1981 when the *National Enquirer* ran a story promoting spirulina as an "all-natural," "safe diet pill." Sales soared as people rushed to obtain the substance the *Enquirer* said contained the amino acid phenylalanine, which "acts directly on the appetite center of the brain." Besides, said the article, "spirulina is an incredible 65 percent protein, making it the most protein-packed food in the world."

Spirulina is generally sold as a food or "food supplement." As a food, spirulina has a history dating at least to the 16th century. One of about 1,500 species of blue-green alga that grow in brackish ponds and lakes, it formed a staple of the Aztecs' diet in Mexico. It was eaten in little cakes and frequently served with a sauce called chilmolli (made of tomatoes, chili peppers and spices). Its popularity lasted until the rule of the Spanish conquistadors, then went the way of many other Aztec customs. In west Africa spirulina has been eaten for hundreds of years.



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Lose Weight & Never Feel Hungry With . . .

Safe Diet Pill

An amazing new natural food supplement — made from plankton — helps you shed pounds fast by taking away your desire to eat. Called spirulina, it contains a substance that acts on the brain's appetite center to switch off your hunger pangs. So you eat less — and lose weight.

Spirulina has been tested and found "safe" by the Food and Drug Administration — and it's available right now in health food stores across America!

'Spirulina is an exciting new way to
ly and safely lose weight," declares
rold Bursell, a top weight-control
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Adds Dr. Dolph Ornstein, president and medical director of the San Francisco Medical Research Center: "The thing about spirulina is that it readily gets into the bloodstream and the body says, 'We're getting the nutrients we need!'"

Taking spirulina also keeps your blood sugar at the proper level — so you don't get hunger pangs, says Dr. Picker.

"There's a hunger center in the hy
thalamus (an area of the brain)
will react to low blood sug
spirulina raises blood su
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Spirulina does contain vitamins and minerals, and it does contain protein. But, if taken in accordance with label directions, the amount of protein derived is negligible. It certainly is not a "super protein." The claim that spirulina is 65 percent protein is meaningless, according to one professor of food science, because protein sources vary in quality and digestability. For example, hair is pure protein but cannot be digested.

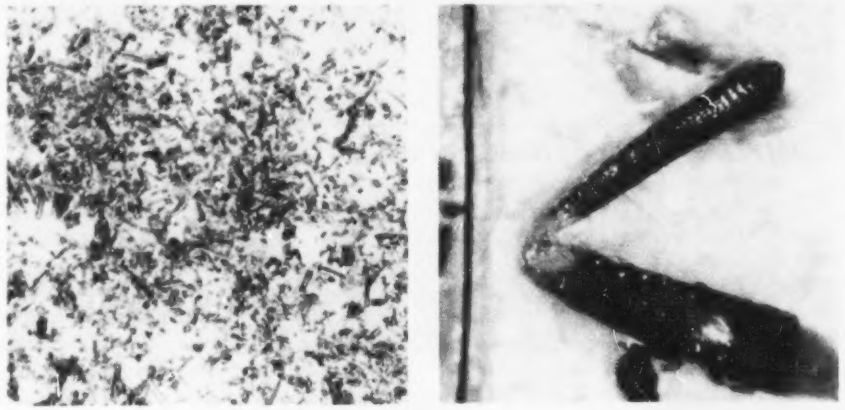
As a food or food supplement, spirulina requires no pre-market approval by FDA. But a claim that it can promote weight loss puts it into the drug category. As such, it must be approved by FDA—lack of approval makes its sale illegal. According to FDA, there is no evidence spirulina is effective as an appetite suppressant. Spirulina does contain phenylalanine as advertised, but it cannot bring about weight loss. In 1979 an FDA advisory panel concluded that there is no medical evidence that the amino acid—which is found in most protein sources—is safe and effective as an appetite suppressant.

Similarly, it is illegal to make therapeutic claims for the alga since there is no medical evidence that spirulina can combat any disease state. Making such claims is what cost MISCORP $225,000.

MISCORP, a multi-million dollar company, is one of the major distributors of spirulina. The company markets the product through 31,000 distributors across the country, generally as a food supplement. But the company also claimed that spirulina had therapeutic effects in cases of diabetes, liver disease and ulcers, and that the product had been "potentized" in a process that "transformed and doubled its effectiveness as a vitamin complex."

Last year the California Department of Health Services Food and Drug Branch began an investigation of MISCORP's marketing of spirulina. State food and drug specialists in two counties spent 12 months accumulating evidence, through inspections of the firm's premises and undercover forays to group sales "parties" held in homes. The state then presented the evidence to the Santa Cruz district attorney's office, which charged MISCORP with making false and misleading claims. MISCORP officials agreed in an out-of-court settlement to pay the fine, the largest ever levied in a California food and drug law case, and to agree not to represent spirulina as having "characteristics which were untrue or misleading" or to say that the product was "potentized." The firm did not acknowledge fault and later told the *San Francisco Chronicle* that the settlement was not an admission of guilt. It is continuing to market the product as a food supplement.

Carol Ballentine is a member of FDA's public affairs staff.



These insects represent an undesirable first. They were found in a shipment of spirulina alga, a food supplement offered for import from Mexico. FDA's San Francisco district lab found some 40,000 insect fragments (mostly from flies) and 20 feather fragments in only three 100-gram samples (that's about 10.5 ounces of sample). In one sample of 3.5 ounces, 25,000 insect fragments were found. The analyst who examined the product said that this was the "heaviest filth load" she had seen in her 20-year career with FDA. The $17,000 shipment has been detained by the district. (The picture on the left has been magnified 4.8 times, the one on the right 50 times.)

Reluctant Repayment

FDA routinely pays for any samples of products it collects during an investigation. It's not routine for the government to get such money back, but it sometimes happens.

A consumer in Sioux City, Iowa, called the FDA office there to complain about a bulging can of Israeli Tehina sauce (a food dressing) purchased at a local market. An FDA investigator then visited the store and found 33 more bulged cans of the sauce. She collected them all as a sample and the government was charged $45.87.

Further investigation by FDA's **Kansas City district** revealed that several months before, the market owner had complained about the bulged cans to the wholesale firm that supplied the Tehina sauce. He had been asked by the wholesaler to destroy the cans and had received a credit for the cost.

The market owner, confronted with this information, claimed the 33 cans purchased by the FDA investigator were from another wholesaler. When it became clear that he couldn't verify this, he agreed to reimburse the government for the $45.87 sample cost plus the $6.72 cost of shipping the sample to the FDA laboratory in Denver.

The laboratory analysis revealed live microorganisms in the sauce, along with hydrogen and carbon dioxide gases.

Undone Donation

A million and a half cans of beets and green beans ended up at the Salvation Army and several food charities—only to be taken away again. The reason wasn't meanness; it was swollen cans.

It all began when a food processor noticed an abnormally high number of swollen cans of green beans and beets in several of its New York plants and complained to Continental Can Co., Stamford, Conn., which had supplied the cans. The can company took samples and found through laboratory analysis that the swells were due to premature corrosion of the can interiors, causing production of hydrogen gas. Reportedly, no microbial growth was found.

The apparent can defects involved 550,000 cans of beets and 945,000 cans of green beans produced by C-B Foods Inc., a division of Curtice-Burns Inc., Rochester, N.Y. Continental Can reimbursed C-B Foods for the affected products and thus became the owner of the canned goods. Since the food apparently was free of microbiological problems, the company decided to donate it to charity. The Salvation Army and a number of federally funded food banks in the Midwest and Northeast were the recipients.

When the donation was made, Continental Can stipulated that the products be served on site, each can examined, and the swollen cans discarded. The food charities, however, distributed the food directly to the public without such an examination. At this point, FDA's **Buffalo district** office heard about the can company's venture through a complaint from someone who had received a swollen can.

An analysis of can samples by FDA's **New York Regional Laboratory** in Brooklyn revealed hydrogen gas, which indicated that the vegetables had reacted with the can lining and caused it to corrode. Microfractures were found in the can lining, and these apparently contributed to the corrosion.

The can company subsequently ordered that all of the remaining products be destroyed because there had been unauthorized, uncontrolled distribution of swollen cans. The company subsequently notified FDA that destruction was carried out at all of the food charities involved.

Save the Scallops

Scallops are considered a choice seafood delicacy, and harvesting these mollusks off the Florida, Georgia and North Carolina coasts has long been important to the states' economies.

Late last December the industry seemed to be headed for trouble. Consumers as far away as Canada were complaining that tiny worms were showing up in the scallops they had purchased.

These were nematodes, a parasite that, as part of its life cycle, lives on and sometimes just in the edible portion (adductor muscle) of the scallop. They are not a health hazard, but they are unappetizing.

About 5 percent of the scallops taken were usually found infected with nematodes, and it was no problem simply to discard these few. But this past January and February as many as half the scallops coming off the boats would have these parasites.

To deal with this, officials of the three states, particularly North Carolina, developed new methods of looking for nematodes and also new methods for removing those found on the surface of the scallops.

FDA's **Atlanta and Orlando district** offices worked with the states to resolve the problem. The increase in nematodes is apparently related to an increase in sea turtles (a host to the parasite) in coastal waters out in the Atlantic.

Defect Action

No matter how they try, food processors cannot remove all the little undesirables that get into foods as they grow in the fields or as they are turned from raw to finished products.

There may be undetectable (to the consumer) pulverized cocoa bean shell in cocoa powder; a bit of grit (also undetectable) in peanut butter; or minute fragments of pit in pitted dates. These are all natural occurrences; they cannot entirely be avoided. They are also normally harmless to human health.

But FDA has limits on how much of these impurities can be permitted in foods. Beyond these tolerances, such substances are at the established "defect action level" (DAL) for the particular food, and FDA then will seize or otherwise prevent the product from being sold.

FDA invoked the DAL for insects in raisins in a shipment that Pyramid Products of Selma, Calif., had sent to Sunray Food Products in New York City.

Sunray had recently received 100 cartons of raisins, to be blended with nuts and dried fruit and marketed as a popular snack food. As each carton came up to be used, Sunray workers examined it for insects. If any were found, the carton was set aside and another one selected that appeared free of insect infestation.

When FDA entered the case, Sunray had used up 25 cartons of "clean" raisins and set aside seven cartons as contaminated. FDA's **New York district** laboratory found moth pupae, moth fragments, dead adult moths and live larvae in the seven set-aside cartons and in another three cartons that Sunray had not yet examined. The inspectors found no other insect activity at the firm, just in the raisins.

Sunray's manager proposed returning the remaining cartons to Pyramid in California, but FDA did not want them to be released back into interstate commerce. FDA asked New York state officials to embargo the raisins while the agency arranged for their seizure. This would place a legal hold on the cartons at Sunray.

While the cartons were under state embargo, however, the firm continued to inspect and use the raisins if they appeared satisfactory. Two cartons were gone when FDA returned with a court order for seizure, which U.S. marshals carried out. The remaining 73 cartons, valued at $2,000, were destroyed by burial in a landfill.

Ironically, FDA inspectors were at Sunray because a retailer had complained that cashews, peanuts, sunflower seeds and the snack blend supplied by Sunray were infested with insects. Checking Sunray's records, the inspectors discovered the retailer had received the foods a year earlier than it claimed. Sunray's manager surmised that the insects had hatched from eggs inevitably present (and below the DAL) in such foods after a long period of incubation and faulty storage by the retailer.

Thawed

The ship "Ultra Freeze" arrived last Dec. 16 at the Port of Miami, loaded with 200 tons of decomposing shrimp. It turned out to have been badly named.

The ship had sailed three months earlier from Guayaquil, Ecuador, headed for the United States with a million-dollar cargo of frozen shrimp. After leaving Ecuador, both its engines and its freezers malfunctioned, delaying the trip and allowing the shrimp to partially thaw. The "Ultra Freeze" docked in Panama for repairs, but apparently the problems were too great because the ship ended up being towed to Miami.

There it encountered more trouble. FDA's **Miami resident post** office had heard about "Ultra Freeze" before it ever arrived, and FDA and Dade county (Florida) inspectors were waiting to check the ship's cargo.

The captain told them the temperature problems began Oct. 16, and he allowed them to copy down the temperatures recorded in the ship's log. This was interrupted by the attorney for the ship's owner, who took possession of the log and refused to permit photos or copies to be made of it. He also threatened to make the inspectors liable if the holds were opened and the contents were later found decomposed.

But the inspectors had seen enough. Their notes already showed that hold temperatures had varied from 29 to 36 degrees Fahrenheit, well above the minimum of 20 degrees set by the state of Florida for frozen foods. The cargo itself showed evidence of thawing, with cartons of shrimp wet and leaking, and open boxes of shrimp completely thawed. The odor of decomposition was apparent as soon as the hatch cover was lifted.

The inspectors were supported by the arrival of a Coast Guard officer who obtained a formal statement from the captain that hold temperatures had risen during the voyage. He also learned that the captain was not licensed to operate in U.S. waters, a technical violation. Another violation was that the owner's attorney had removed the ship's log when he went ashore.

In addition to FDA detention, Dade county health officials put an immediate "stop sale" order on the shrimp and condemned and later destroyed 60,000 pounds (value $200,000) that was badly thawed and decomposed. The remainder is still under detention by FDA.

Food Explosion

What does one do with a can of commercially processed food that "explodes" or is bulging at the seams? Those who are wise call FDA.

Pizza parlor owners in three states called their FDA district offices to report swelled cans of pizza-cut mushrooms. Analysis of samples by the **Cincinnati district** lab revealed that the mushrooms were decomposing and contained living microorganisms, indicating they may have been underprocessed. Inadequate thermal processing of canned vegetables and other low-acid foods can permit the development of botulinal toxin, which when eaten can cause botulism poisoning.

Cincinnati district investigators inspected the manufacturer, Heskett Foods Inc., Columbus, Ohio, and found a number of deficiencies in the firm's processing procedures. When informed of the problems, company officials agreed to make corrections. The company also recalled all pizza-cut mushrooms that might have been underprocessed—approximately 10,000 cases.

An account of "exploding" tomatoes didn't warrant an inspection but did go down in FDA's record books for future reference.

A woman from Kensington, Md., called the agency's headquarters office to report that a can of tomatoes had exploded after being perforated with a can opener. She wanted to know if it was possible for tomatoes to contain botulinal toxin.

She was told that it was not impossible but was extremely unlikely since the high acid content of tomatoes inhibited the growth of botulinum organisms. Her complaint then became part of FDA's record on the firm that produced the tomatoes.

A possible cause of the can's explosion was hydrogen gas produced by a reaction between the acid in the tomatoes and the can's metal lining. In this type of reaction, which may occur over time, metallic salts may also be formed, which can impart a metallic taste to the food. High-acid products are frequently, but not always, processed in cans lined with a coating to prevent this type of chemical reaction. Swollen cans of high-acid products may also be caused by bacterial growth. Some bacteria are capable of growing in an acid environment and subsequently raising the pH to a level where botulinum organisms can grow. However, this does not occur often.

A swollen can may also indicate bacterial contamination of the food. Some bacteria will produce hydrogen gas but more frequently produce carbon dioxide. Swelling of cans containing low-acid foods is more likely to indicate bacterial contamination and a potential danger to health. Consumers would be wise to check their pantries frequently for swollen cans, be sure not to consume the product, and if possible let FDA know.

Enough Is Enough

A group of restaurant owners in Chattanooga, Tenn., doing business as the Chattanooga Restaurant Supply Corp., own and operate a cooperative food warehouse in that city. This arrangement enables them to buy food and other supplies at lower cost in bulk for distribution to the various locations of the members.

For six years, FDA's **Nashville district** office made routine surveillance inspections (10 in all) of the co-op warehouse. Each time the inspectors found "widespread and continuing evidence" of rodent activity in and around the warehouse. At times the conditions might be a bit better or worse than at others, but never was the warehouse the way it should be. The co-op and its management were cited, but when FDA went back the overall conditions were unchanged.

During 1980 FDA made two inspections and found seventeen 50-pound bags of flour, eleven 25-pound bags of dried lentils, and five 50-pound bags of doughnut mix that were gnawed by rodents, contaminated by rodent filth, or being held under conditions that would allow them to be contaminated.

Enough is enough, said the Nashville office, and took the corporation to court for violations of the Food, Drug, and Cosmetic Act. Enough is enough, agreed the U.S. District Court for the Eastern District of Tennessee, which levied the maximum fine of $3,000 on the co-op and placed its general manager, Felix Inglis, on probation for two years after he pleaded guilty to all three counts.

—Compiled and written by Carol Ballentine, Louise Fenner and Richard Thompson.

Seizures and Postal Service Cases

FILED SEIZURE ACTIONS

charge violations of the Federal Food, Drug, and Cosmetic Act and are initiated based upon FDA recommendations. A seizure action is commenced by the filing in the U.S. district court where the goods are located. A U.S. marshal is then directed by the court to take possession of the goods, removing the product from commerce, until the matter is resolved.

A total of 10 actions to remove from the consumer market products charged to be violative was reported in April. These actions included 8 of foods, 5 involving charges concerning contamination, spoilage or insanitary handling, and 3 involving food additives. Others included 2 of drugs.

PRODUCT, DISTRICT & DATE FILED	FIRM & PLACE OF BUSINESS	CHARGES
	FOOD/Contamination, Spoilage, Insanitary Handling	
Flour, corn flour and rice/U.S. District Court for the District of Massachusetts 2/2/82	Bay State Food Co. Inc./Woburn, Mass.	Products held under insanitary conditions, and one lot contains rodent filth.
Grapefruit sections, canned/U.S. District Court for the Eastern District of Missouri 1/21/82	Morris Canning Co./Winter Haven, Fla.	Product held in cans which are swollen and leaking.
Scallops/U.S. District Court for the District of Nevada 1/28/82	Shipped from Salem, Ore.	Product contains decomposed scallops.
Soup base and other foodstocks/U.S. District Court for the Western District of Washington 1/29/82	Yick Fung/Seattle, Wash.	All lots have been held under insanitary conditions, and some lots contain insect filth.
Sugar and other foodstocks/U.S. District Court for the Eastern District of Tennessee 3/2/82	Smith & Son Wholesale Co. Inc./Tullahoma, Tenn.	Products were held under insanitary conditions.
	FOOD ADDITIVES	
Coco Rico coconut beverage/U.S. District Court for the District of Puerto Rico 3/11/82	Coco Rico Inc./Naguabo, Puerto Rico (coconut concentrate component manufacturer)	Product contains the non-conforming food additive potassium nitrate.
Coco Rico coconut beverage/U.S. District Court for the District of Puerto Rico 3/11/82	Coco Rico Inc./Naguabo, Puerto Rico (coconut concentrate component manufacturer)	Product contains the non-conforming food additive potassium nitrate.
Kokito coconut beverage/U.S. District Court for the District of Puerto Rico 3/11/82	Coco Rico Inc./Naguabo, Puerto Rico (coconut concentrate component manufacturer)	Product contains the non-conforming food additive potassium nitrate.
	DRUGS/Human Use	
Reserpine hydralazine HCl, hydrochlorothiazide tablets/ U.S. District Court for the District of New Jersey 1/14/82	Zenith Laboratories/Northvale, N.J.	Strength differs from and quality falls below U.S.P. standards, since product failed U.S.P. content uniformity test for reserpine active ingredient.
WANS suppositories and pyrilamine maleate component/U.S. District Court for the District of Puerto Rico 1/11/82	Alcon Laboratories Inc./Humacao, Puerto Rico	Product is a new drug without an effective approved New Drug Application.

U.S. POSTAL SERVICE

actions taken in medical cases as authorized in the Mail Fraud Statute (18 U.S.C. 1341) and/or the False Representa
tion Statute (39 U.S.C. 3005) as reported by the Chief Postal Inspector.

Complaints Filed by Law Department Under 39 U.S.C. (False Representation)

November 4, 1981: **Formula Four Inc.,** P.O. Box 81262, Chamblee, Ga. Advertising and sale through the mail of the product "Jennifer Lord Formula #714." The ad states, in part, "is the first natural, nonsurgical way to enlarge your breasts that makes sense. It utilizes the body's own breast development mechanism to improve your natural appearance and self-confidence . . . best of all, it works!"

November 4, 1981: **Athena Products Ltd.,** P.O. Box 757, Decatur, Ga. Advertising and sale through the mail of the product "The Cellussage System." The ad states, in part, "would you spend an hour to get rid of a lifetime of cellulite? Experience immediate cellulite elimination with the Cellussage System . . . this unique system can even draw out cellulite deposits that have been trapped in your legs, thighs, buttocks, and arms for years."

November 4, 1981: **Body Science,** 20 Medford Ave., Patchogue, N.Y. Advertising and sale through the mail of the product "DMG-15," representing the ability to "prevent infection and disease, even add years to your life! With DMG-15, the Supernutrient Pill that can significantly improve your life and give you energy, stamina and endurance at work, at play, or at night with your spouse."

November 5, 1981: **Lanzette Laboratories,** P.O. Box 25677, Chicago, Ill. Adv
tising and sale through the mail of the product "Lanzette Device Ha
Removal." The ad states, in part, "painless, inexpensive, non-elect
method for removing hair from the face, lips, chin, arms, legs . . . ."

November 5, 1981: **Formula Four Inc.,** P.O. Box 81262, Chamblee, Ga. Adv
tising and sale through the mail of the product "Total Control," rep
senting the ability to "get rid of cellulite immediately."

November 10, 1981: **Nature's Harvest Inc.,** 95 M South Hoffman Lane, Cent
Islip, N.Y. Advertising and sale through the mail of the product "G
Chromium Tablets." The ad states, in part, "taking GTF as part of yo
nutritional plan can help eliminate the possibilities that you will suf
from a GTF deficiency."

November 10, 1981: **Nature's Harvest** 95 M South Hoffman Lane, Central Isl
N.Y. Advertising and sale through the mail of the product "Sup
Nucleic Acid Complex," representing the ability to "help the body fig
against the effects of aging and disease the 'natural' way."

False Representation Orders Issued by Judicial Officer Under 39 U.S.C. 3005

December 11, 1981: Against **Cosvetic Labs,** P.O. Box 49303, Atlanta, Ga. Satisfactory evidence was presented to the Postal Service that Cosvetic Labs and their agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Youth Extension System," representing the ability to "stay young by using the complete system."

December 11, 1981: Against **Cosvetics,** P.O. Box 53098, Atlanta, Ga. Satisfactory evidence was presented to the Postal Service that Cosvetics and their representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the products "Dismutase, Neocel Tablets and Cream, and GTF-Glucose Tolerance Factor," representing the ability to "protect cells from free radicals, improve the cell function and GTF helps activate insulin to remove sugar from bloodstream."

December 11, 1981: Against **Frederick French,** 30 Montrose Ave., New York, N.Y. Satisfactory evidence was presented to the Postal Service that Frederick French and their agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Living Fluid and Living Creme," representing the ability to "enlarge your bosom . . . be big busted beautiful in an era
small bosomed women . . . gain up to 6 inches and 3 cup sizes now!"

December 11, 1981: Against **Specialty Diet Sales Inc.,** 1919 Broadhollow R
Farmingdale, N.Y. Satisfactory evidence was presented to the Pos
Service that Specialty Diet Sales Inc. and their representatives a
engaged in conducting a scheme or device to obtain money by means
false representation. The firm was advertising the product "Fat Melti
Factor." The ad states, in part, "peel off a pound a day without missing
single meal! You must see dramatic results in just 24 hours . . . lose up
6 pounds the first 48 hours. Lose up to 10 pounds the first 7 days . . .
your money back!"

December 14, 1981: Against **Renee Renoir,** 1626 N. Wilcox, Hollywood, Cal
Satisfactory evidence was presented to the Postal Service that Ren
Renoir and their agents are engaged in conducting a scheme or device
obtain money by means of false representation. The firm was advertisi
the product "Le Grand Big Bosom Creme and Big Bosom Le Gra
Pills," representing the ability to "enlarge your bosom . . . increase yo
bustline up to 6 inches and 3 cup sizes!"

Notices of Judgment

NOTICES OF JUDGMENT on Seizure Actions

FOOD/Poisonous and Deleterious Substance

Non-dairy creamer, at Belle Plaine, Dist. Minn.

Charged 10-19-81: while held by Valley Processors Inc., Belle Plaine, Minn., who manufactured the article using interstate coconut oil, the article contained the added poisonous or deleterious substance salmonella microorganisms, which might render the article injurious to health; 402(a)(1). Default decree ordered destruction. (F.D.C. No. 63569; S. No. 81-338-558; N.J. No. 1)

FOOD/Contamination, Spoilage, Insanitary Handling

Beans, pinto, dried, at Lubbock, N. Dist. Texas.

Charged 11-12-80: while held by Armstrong Moving & Storage Inc., Lubbock, Texas, the article contained rodent filth and had been held under insanitary conditions; 402(a)(3) and (4). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63219; S. No. 80-265-353 et al.; N.J. No. 2)

Flour, high gluten, at Brooklyn, E. Dist. N.Y.

Charged 10-20-81: while held by Joseph Fragola Inc., Brooklyn, N.Y., the article contained insect and rodent filth, and had been held under insanitary conditions; 402(a)(3) and (4). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63561; S. No. 81-337-850; N.J. No. 3)

Orange pieces, mandarin, canned, at Dallas, N. Dist. Texas.

Charged 10-16-81: while held for sale, the article was contained in swollen cans; 402(a)(3). Default decree ordered destruction. (F.D.C. No. 63564; S. No. 81-266-659; N.J. No. 4)

Pancake mix, at Catano, Dist. Puerto Rico.

Charged 10-20-81: while held for sale, the article contained insect filth; 402(a)(3). Default decree ordered destruction. (F.D.C. No. 63573; S. No. 81-281-742; N.J. No. 5)

Rice, macaroni products, cheese, and **other food stocks,** at Seattle, W. Dist. Wash.

Charged 10-13-81: while held by Pacific Food Importers, Seattle, Wash., some of the articles contained rodent and/or insect filth, and all of the articles had been held under insanitary conditions; 402(a)(3) and (4). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63575; S. No. 81-278-802; N.J. No. 6)

FOOD/Economic and Labeling Violations

"Honey," at Russellville, E. Dist. Ark.

Charged 10-23-81: when shipped from Dekalb, Miss., the article, labeled in part "Natures-Natural Pure Raw Honey Packed for Big Giant Foods . . . Oklahoma City, Okla.," had had glucose syrup substituted for honey 402(b)(2); the article's labeling regarding content and distributor was false and misleading since the article was not pure honey and was not packed for Big Giant Foods 403(a)(1); and the article was also in violation of the Fair Packaging and Labeling Act since the quantity of contents statement was not expressed as required by regulations; 15 U.S.C. 1453(a)(3)(A)(i). Default decree authorized donation to a charitable institution. (F.D.C. No. 63574; S. No. 81-221-980; N.J. No. 7)

"Maple" syrup, at DeKalb, S. Dist. Miss.

Charged 7-27-81: while held by Paul Pilgrim Syrup Co., DeKalb, Miss., who prepared the article using interstate corn syrup, the article, labeled in part "Wild Mountain Brand Maple Syrup . . . Wild Mountain Syrup Co. . . . DeKalb, Miss. . . . Tapped In Vermont," had had corn syrup substituted for maple syrup—402(b)(2); the article's labeling was false and misleading as to the product's name "Maple Syrup"; the article failed to meet the definition and standard of identity for maple syrup since the article contained corn syrup 403(a)(1), 403(g)(1); and the article was also in violation of the Fair Packaging and Labeling Act since the quantity of contents statement was not expressed as required by regulations 15 U.S.C. 1453(a)(3)(A)(i). Default decree authorized donation to charitable institutions for use only. (F.D.C. No. 63515; S. No. 81-275-808 et al.; N.J. No. 8)

ANIMAL FEED

Animal feed containing diethylstilbestrol, at Brownsdale, Dist. Minn.

Charged 5-28-80: while held for sale, the article was an animal feed containing the non-conforming new animal drug diethylstilbestrol since no approval of a New Animal Drug Application was in effect with respect to the use or intended use of the drug in animal feed; 501(a)(6). Default decree ordered destruction. (F.D.C. No. 63035; S. No. 80-217-245; N.J. No. 9)

DRUGS/Human Use

Allopurinol tablets, chlorpropamide tablets, chlorthalidone tablets, diethylpropion HCl tablets, doxylamine succinate with B_6 tablets, furosemide tablets, hydroxyzine HCl tablets, hydroxyzine pamoate capsules, metronidazole tablets, prochlorperazine capsules, triamterene with hydrochlorothiazide capsules, and **trimethoprim with sulfamethoxazole tablets,** at Rockville Centre, E. Dist. N.Y.

Charged on or about 4-29-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). Consent decree ordered destruction. (F.D.C. No. 62977; S. No. 80-200-005 et al.; N.J. No. 10)

Chlorothiazide tablets, at Santa Clara, N. Dist. Calif.

Charged 1-26-81: when shipped by Camall Co., Detroit, Mich., the article, labeled in part "Chlorothiazide, U.S.P. 500 mg . . . Tablets Distributed By Sheraton Laboratories, Santa Clara, Calif. . . . Camall Company, Detroit, Mich.," was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (F.D.C. No. 63275; S. No. 81-150-751; N.J. No. 11)

Chlorthalidone tablets, and **other specified drugs,** at Cincinnati, S. Dist. Ohio.

Charged 12-23-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). Default decree ordered destruction. (F.D.C. No. 63277; S. No. 81-272-406 et al.; N.J. No. 12)

Chlorthalidone tablets, hydroxyzine HCl tablets, hydroxyzine pamoate capsules, and **trimethoprim with sulfamethoxazole tablets,** at San Diego, S. Dist. Calif.

Charged 2-13-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The article was claimed by the shipper who denied the charges. Pursuant to stipulation, the action was transferred to the District of New Jersey for consolidation for trial with a similar action. Subsequently, a consent decree ordered destruction. (F.D.C. No. 62816; S. No. 80-208-377 et al.; N.J. No. 13)

Diethylpropion hydrochloride tablets, hydroxyzine hydrochloride tablets, and **other specified drugs,** at Cumberland, Dist. Md.

Charged 10-30-79: when shipped by Pharmadyne Laboratories Inc., Hackensack, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was transferred to the Eastern District of New York for trial with a similar action. Subsequently, a consent decree ordered the articles destroyed. (F.D.C. No. 62556; S. No. 79-206-283 et al.;

N.J. No. 14)

Diethylpropion HCl tablets, furosemide tablets, and **other specified drug stocks,** at Chicago, N. Dist. Ill.
Charged 3-27-79: when shipped by Pharmadyne Laboratories Inc., Hackensack, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper. Pursuant to stipulation, the action was removed to the Eastern District of New York for consolidation for trial with a similar action. Subsequently, a consent decree ordered destruction. (F.D.C. No. 62210; S. No. 79-111-834; N.J. No. 15)

Furosemide tablets, hydroxyzine HCl tablets, prochlorperazine capsules, hydroxyzine pamoate capsules, metronidazole tablets, allopurinol tablets, diethylpropion HCl tablets, chlorpropamide tablets, and **trimethoprim with sulfamethoxazole tablets,** at Brooklyn, E. Dist. N.Y.
Charged 4-16-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). Consent decree ordered destruction. (F.D.C. No. 62968; S. No. 80-140-637; N.J. No. 16)

Spironolactone with hydrochlorothiazide tablets, at Valley Stream, E. Dist. N.Y.
Charged 7-5-81: when shipped by Pharmadyne Laboratories Inc., Hackensack, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). Consent decree ordered destruction. (F.D.C. No. 62323; S. No. 79-139-759; N.J. No. 17)

DRUGS/Veterinary

Diethylstilbestrol implant pellets, at Nowata, N. Dist. Okla.
Charged 6-18-80: while held for sale, the article was a new animal drug and no approval of a New Animal Drug Application was in effect with respect to its use or intended use; 505(a). Default decree ordered destruction. (F.D.C. No. 63079; S. Nos. 80-211-756/7; N.J. No. 18)

Diethylstilbestrol implant pellets, at Wayne, W. Dist. Okla.
Charged 6-11-80: while held for sale, the article was a new animal drug and no approval of a New Animal Drug Application was in effect with respect to its use or intended use; 501(a)(5). Default decree ordered destruction. (F.D.C. No. 63079; S. No. 80-211-495; N.J. No. 19)

Diethylstilbestrol implant pellets, three seizure actions, at Kingfisher, W. Dist. Okla.; Tribune, Dist. Kan.; and Oklahoma City, W. Dist. Okla.
Charged on or about 5-21-80, 5-22-80, and 1-9-81: while held for sale, the articles were new animal drugs and no approval of a New Animal Drug Application was in effect with respect to their use or intended use; 501(a)(5). Default decrees ordered destruction. (F.D.C. Nos. 63014, 63051, 63274; S. Nos. 80-211-585, 80-250-724, 81-209-999; N.J. No. 20)

MEDICAL DEVICES

X-ray control panel, Traceray III, at Miami, S. Dist. Fla.
Charged 10-10-79: the article, which had been manufactured by Western States Supply Ltd., Pueblo, Colo., was dangerous to health when used as directed because the article would emit radiation beyond the pre-set exposure time—502(j); and the article's quality fell below its purported quality—501(c). Default decree ordered destruction. (F.D.C. No. 62519; S. No. 79-166-429; N.J. No. 21)

X-ray control panel, Traceray III, at Wasilla, Dist. Alaska.
Charged 11-7-79: the article, which had been manufactured by Western States Supply Ltd., Pueblo, Colo., was dangerous to health when used as directed because the device would emit radiation beyond the pre-set exposure time—502(j); the accompanying labeling was false and misleading in claiming compliance with the regulation's standards and in claiming that the device would deliver the radiation exposure stated in the instruction manual—502(a); and the article's quality fell below its purported quality—501(c). Default decree ordered destruction. (F.D.C. No. 62578; S. No. 79-152-707; N.J. No. 22)

X-ray control panel, Traceray III, with collimator, at Troutdale, Dist. Ore.
Charged 10-17-79: the article, which had been manufactured by Western States Supply Ltd., Pueblo, Colo., was dangerous to health when used as directed because the article would emit radiation beyond the pre-set exposure time—502(j); the accompanying labeling was false and misleading in claiming compliance with the regulation's standards, and in claiming that the device would deliver the radiation exposure stated in the instruction manual—502(a); and the article's quality fell below its purported quality—501(c). Consent decree authorized release to the owner/possessor for reconditioning. (F.D.C. No. 62576; S. No. 79-176-161; N.J. No. 23)

X-ray system, Traceray IV, at El Toro, C. Dist. Calif.
Charged 10-5-79 and amended 10-29-79: the article, which had been manufactured by Western States Supply Ltd., Pueblo, Colo., was dangerous to health when used as directed because the article would emit radiation beyond the pre-set exposure time—502(j); the accompanying labeling was false and misleading in claiming compliance with the regulation's standards, and in claiming that the device would deliver the radiation exposure stated in the instruction manual—502(a); and the article's quality fell below its purported quality—501(c).

The article was claimed by the possessor, who moved for summary judgment claiming that he owned a Traceray III which met all established standards. Meanwhile, the government had filed its amended complaint correcting the typographical error so that the article was correctly alleged to be a Traceray III. The government opposed the claimant's motion to dismiss. Subsequently, a consent decree of condemnation authorized release of the article to the claimant for reconditioning. (F.D.C. No. 62586; S. No. 79-214-644; N.J. No. 24)

X-ray system, Traceray III, at Baudette, Dist. Minn.
Charged 10-15-79: the article, which had been manufactured by Western States Supply Ltd., Pueblo, Colo., was dangerous to health when used as directed because the device would emit radiation beyond the pre-set exposure time—502(j); the accompanying labeling was false and misleading in claiming compliance with the regulation's standards, and in claiming that the device would deliver the radiation exposure stated in the instruction manual—502(a); and the article's quality fell below its purported quality—501(c).

The article was claimed by the possessor who denied the charges. The possessor subsequently withdrew his claim and answer because the article had been sold. A consent decree of condemnation was entered into by the new owner; the decree authorized release for reconditioning. (F.D.C. No. 62615; S. No. 79-218-507; N.J. No. 25)

X-ray system, Traceray III, at Eagan, Dist. Minn.
Charged 10-2-79: the article, which had been manufactured by Western States Supply Ltd., Pueblo, Colo., was dangerous to health when used as directed because the article would emit radiation beyond the pre-set exposure time—502(j); the accompanying labeling was false and misleading in claiming compliance with the regulation's standards, and in claiming that the device would deliver the radiation exposure stated in the instruction manual—502(a); and the article's quality fell below its purported quality—501(c).

The article was claimed by the possessor who admitted the charges and requested release under bond for bringing into compliance. A form of consent decree for release for bringing into compliance was provided the claimant. When there was no further interest on the part of the claimant, the government moved for judgment on the pleadings. The court granted the government judgment on the pleadings and ordered the article de-

stroyed. (F.D.C. No. 62614; S. No. 79-202-844; N.J. No. 26)

X-ray system, Traceray III, at Johnstown, W. Dist. Pa.

Charged 10-12-79: the article, which had been manufactured by Western States Supply Ltd., Pueblo, Colo., was dangerous to health when used as directed because the article would emit radiation beyond the pre-set exposure time—502(j); and the article's quality fell below its purported quality—501(c). Default decree ordered forfeiture of article. (F.D.C. No. 62598; S. No. 79-231-141; N.J. No. 27)

X-ray systems, Traceray III, 11 seizure actions, at Montgomery, M. Dist. Ala.; Aspen, Dist. Colo.; Los Altos, N. Dist. Calif.; San Jose, N. Dist. Calif.; Battleground, W. Dist. Wash.; Mt. Vernon, W. Dist. Wash.; Marysville, E. Dist. Calif.; Houston, S. Dist. Texas; Lake Jackson, S. Dist. Texas; Baytown, S. Dist. Texas; and Richmond, E. Dist. Ky.

Charged 10-18-79, 10-2-79, 10-5-79, 10-5-79, 10-16-79, 10-16-79, 10-10-79, 11-19-79, 11-19-79, 11-19-79, 10-31-79: the articles, which had been manufactured by Western States Supply Ltd., Pueblo, Colo., were dangerous to health when used as directed because the devices would emit radiation beyond the pre-set exposure time—502(j); the accompanying labeling was false and misleading in claiming compliance with the regulation's standards, and in claiming that the devices would deliver the radiation exposure stated in the instruction manual—502(a); and the articles' quality fell below their purported quality—501(c). Consent decrees authorized release to the owners/possessors for reconditioning. (F.D.C. Nos. 62486, 62530, 62550, 62551, 62563, 62567, 62573, 62627, 62628, 62629, 62633; S. Nos. 79-164-168, 79-195-746, 79-150-337, 79-150-338, 79-176-824, 79-152-759, 79-180-113, 79-192-648, 79-192-649, 79-192-647, 79-131-576; N.J. No. 28)

X-ray systems, Traceray III, five seizure actions, at Montgomery, M. Dist. Ala.; Montgomery, M. Dist. Ala.; Jacksonville, M. Dist. Fla.; Olympia, W. Dist. Wash.; and Smithfield, S. Dist. Ohio.

Charged 10-18-79, 10-18-79, 10-24-79, 10-16-79, 10-22-79: the articles, which had been manufactured by Western States Supply Ltd., Pueblo, Colo., were dangerous to health when used as directed because the devices would emit radiation beyond the pre-set exposure time—502(j); the accompanying labeling was false and misleading in claiming compliance with the regulation's standards, and in claiming that the devices would deliver the radiation exposure stated in the instruction manual—502(a); and the articles' quality fell below their purported quality—501(c). Default decrees ordered destruction. (F.D.C. Nos. 62487, 62488, 62541, 62569, 62591; S. Nos. 79-164-169, 79-158-591, 79-197-815, 79-212-641, 79-186-057; N.J. No. 29)

X-ray systems, Traceray III, 16 seizure actions, at Spokane, E. Dist. Wash.; Yakima, E. Dist. Wash.; Tacoma, W. Dist. Wash.; Seattle, W. Dist. Wash.; Seattle, W. Dist. Wash., Bellingham, W. Dist. Wash.; Tacoma, W. Dist. Wash.; Reynoldsburg, S Dist Ohio; Columbus, S. Dist. Ohio; Greensburg, W. Dist. Pa.; Pittsburg, W. Dist. Pa.; Minneapolis, Dist. Minn.; St. Paul, Dist. Minn.; Lewisport, W. Dist. Ky.; Danville, E. Dist. Ky.; and Frankfort, E. Dist. Ky.

Charged 10-19-79, 10-19-79, 10-16-79, 10-16-79, 10-16-79, 10-16-79, 10-16-79, 10-22-79, 10-22-79, 10-12-79, 10-12-79, 10-2-79, 10-2-79, 10-15-79, 10-31-79, 10-31-79: the articles, which had been manufactured by Western States Supply Ltd., Pueblo, Colo., were dangerous to health when used as directed because the devices would emit radiation beyond the pre-set exposure time—502(j); the accompanying labeling was false and misleading in claiming compliance with the regulation's standards, and in claiming that the devices would deliver the radiation exposure stated in the instruction manual—502(a); and the articles' quality fell below their purported quality—501(c). Consent decrees authorized release to owners/possessors for reconditioning. (F.D.C. Nos. 62535, 62536, 62560, 62564, 62565, 62566, 62568, 62595, 62596, 62599, 62602, 62605, 62618, 62624, 62635, 62636; S. Nos. 79-212-043, 79-153-192, 79-152-958, 79-152-955, 79-152-953, 79-152-952, 79-152-957, 79-186-074, 79-112-332, 79-204-547, 79-204-544, 79-202-808, 79-202-806, 79-131-935, 79-131-574, 79-131-893; N.J. No. 30)

NOTICE OF JUDGMENT on Criminal Action

Chattanooga Restaurant Supply Corp., and **Felix B. Inglis,** secretary and general manager, Chattanooga, E. Dist. Tenn.

Charged 12-1-81: flour, dried lentils and cake donut mix had been held under insanitary conditions in a building accessible to rodents and had been contaminated with rodent filth; 402(a)(3) and (4). The individual pleaded guilty and was placed on probation for two years. The corporation pleaded guilty and was fined $3,000. (F.D.C. No. 63454; S. No. 80-229-558 et al.; N.J. No. 31)

NOTICES OF JUDGMENT on Injunction Actions

Earthco, and **Alfonso G. Nunez,** president, Westlake Village, C. Dist. Calif.

Charged 10-78 in a complaint for injunction: that the defendants had manufactured, processed, packed, labeled, held, promoted and distributed articles of food and drugs known as "Apricaps" and "Raw Natural Apricot Kernels"; that "Apricaps" consisted of gelatin capsules containing ground apricot kernels and was labeled in part "APRICAPS, A Food for Dietary Supplementation . . . contain . . . Amygdalin, a naturally occurring cyanogenetic glucoside (sometimes unofficially referred to as Vitamin B-17) . . . Apricot kernels may be toxic . . . Earthco, Westlake Village, Calif."; that the gelatin capsules of the "Apricaps" were manufactured outside the state of California and had been shipped in interstate commerce; that "Raw Natural Apricot Kernels" consisted of apricot kernels intended for human consumption in packages labeled in part "Raw, Natural Apricot Kernels (seeds) . . . Can Be Toxic Do Not Overeat As Individual Tolerance Varies—Over Indulgence Will Cause Nausea And Other Symptoms—Very Low Quantities May Cause Reactions"; that FDA analyses revealed that the defendants' "Apricaps" released hydrocyanic acid equivalent to 2,281-2,986 ppm of cyanide; and that the defendants' "Raw Natural Apricot Kernels" contained approximately 4 percent amygdalin which was the equivalent of approximately 2,300 ppm of hydrocyanic acid; that the defendants' "Apricaps" contained the nonconforming food additive amygdalin; that the "Apricaps" and "Raw Natural Apricot Kernels" were unfit for food by reason of their content of hydrogen cyanide; that the labeling of "Apricaps" contained false and misleading claims of nutrient and special dietary properties; that the labeling of both articles lacked adequate directions for use for their intended purposes in the treatment or prevention of cancer; that their labeling lacked adequate warnings against unsafe use since the articles were not fit for human consumption; that the articles' labels lacked the prescription legend; that, if the defendants were forced by an injunction to distribute the articles with labeling for the use for which the articles were intended (i.e., the treatment or prevention of cancer), the articles would be new drugs without effective approved New Drug Applications; and that the defendants had been advised on a number of specified occasions that their distribution of "Apricaps" was in violation of the law; 402(a)(2)(C), 402(a)(3), 403(a), 502(f)(1), 502(f)(2), 503(b)(4), 505(a).

The defendants denied the charges. Since they had "no intention of selling the articles as anything but foods," they also filed their consent to an injunction from selling any apricot kernel products for any drug uses or purposes. In granting the government a preliminary injunction against the defendants, the court said:

"In this action, the United States seeks to preliminarily enjoin defendants, Earthco and its president, Alfonso G. Nunez, from shipping into interstate commerce the products 'Raw Natural Apricot Kernels' and 'Apricaps.' The government asserts that such shipment violates the Federal Food, Drug, and Cosmetic Act.

" 'Raw Natural Apricot Kernels' are, as their name suggests, simply unprocessed apricot kernels. 'Apricaps' consist of ground apricot kernels packaged in gelatin capsules.

"The heart of the government's claim is that defendants' products are toxic because their ingestion assertedly can lead to cyanide poisoning. Apricot kernels contain the chemical amygdalin as well as enzymes which, in the presence of moisture, act to release cyanide from the amygdalin. Cyanide, of course, is a toxic substance. The government contends that a person can consume a sufficient quantity of defendants' products to cause either immediate or chronic cyanide poisoning. The defendants admit that ingestion of their products can result in the release of cyanide into the consumer's system, but contend, among other things, that a person could not ingest a sufficient quantity of the products to pose any danger to himself.

"Apricot kernels, and their component amygdalin, are used by some persons in the treatment of cancer. Amygdalin is chemically similar to, though distinct from, Laetrile. Laetrile is another substance used by some in the treatment of cancer.

"The government requests an injunction that is specifically authorized by statute. 21 U.S.C. § 322(a). Therefore, in ruling on this motion for a preliminary injunction, the court need not apply the equitable tests traditionally considered when deciding a controversy between private parties. Rather, if a violation of the Food, Drug, and Cosmetic Act is demonstrated, an injunction must be forthcoming. *United States* v. *Diapulse Corporation of America,* 457 F.2d 25 (2nd Cir. 1972).

"The key issue on this motion is whether 'Apricaps' and 'Raw Natural Apricot Kernels' are 'drugs' within the meaning of the Act. In relevant part, the Act provides that the term 'drug' shall include 'articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals.' 29 U.S.C. § 321(g)(1)(B). 'It is well settled that the intended use of a product may be determined from its label, accompanying labeling, promotional materials, advertising and any other relevant source.' *United States* v. *Article . . . Consisting of 216 Cartoned Bottles,* 409 F. 2d 734, 739 (2nd Cir. 1969) (citing several circuit court opinions).

"The evidence demonstrates that the defendants have marketed 'Apricaps' and 'Raw Natural Apricot Kernels' with the intent that they be used in the treatment of cancer, and therefore these products must be deemed 'drugs' for the purposes of the Act. In September 1977, the defendants sent a promotional flyer to owners of health food stores. The flyer promoted the sale of 'Apricaps.' . . . The gist of the flyer is that persons should purchase 'Apricaps' (and by inference, 'Raw Natural Apricot Kernels') because they contain Laetrile. In addition, the reference to 'the great Laetrile controversy' can only refer to the fact that some persons believe Laetrile is useful in the treatment of cancer. The import of the flyer, therefore, is that persons should purchase 'Apricaps' and 'Raw Natural Apricot Kernels' for the treatment of cancer. Moreover, the evidence demonstrates that defendant Nunez knows that persons have purchased his products as a cancer cure. This suggests, independent of the flyer, that the defendants intend their products to be used as a drug.

"The next question is whether defendants' products are 'new drugs' within the meaning of the Act. A 'new drug' may not be introduced or delivered for introduction into interstate commerce unless a new drug application for that drug has been approved by the Secretary of Health, Education, and Welfare. 21 U.S.C. § 355(a). . . . The declarations of experts in the field of toxicology, submitted by both sides, demonstrater that apricot kernels are not generally recognized among experts as a drug that is both safe and effective under any conditions. Thus, 'Apricaps' and 'Raw Natural Apricot Kernels' are 'new drugs.'

"Apparently, there exists no approved new drug application for either apricot kernels or 'Apricaps.' The evidence also indicates that defendants are distributing their products in interstate commerce. It follows, therefore, that since the products are 'new drugs,' the defendants must be enjoined from introducing, or delivering for introduction, into interstate commerce the drugs 'Apricaps' and 'Raw Natural Apricot Kernels' until a New Drug Application has been approved by the Secretary of Health, Education, and Welfare."

Subsequently, for the purposes of compromise and in advance of a final hearing, defendant entered into a consent decree of permanent injunction enjoining the introduction of the drugs "Apricaps" and "Raw Natural Apricot Kernels" until a New Drug Application had been approved. (Inj. No. 862; S. No. 78-105-125 et al.; N.J. No. 32)

Mark Medica Inc., Albert R. Flint, president, and **Edward C. Martinez,** plant manager, Buffalo, W. Dist. N.Y.

Charged 11-14-78 in a complaint for injunction: that the defendants, at their Buffalo, N.Y., plant, manufactured, processed, packaged, labeled, held and distributed in interstate commerce various surgical apparatus (including sponges, catheter trays and neurological strips) purported to be sterile and intended for use in neurosurgery, laparotomy and other surgical procedures; that the defendants manufactured, processed, packaged and/or labeled a number of such devices while they were held for sale after interstate shipment of components; that the devices had been prepared, packed and held under insanitary conditions whereby they might have been rendered injurious to health; that certain lots of catheter trays fell below their purported quality and their labeling was false and misleading because the catheter trays were not as sterile as they were represented to be; that FDA inspections disclosed a number of specified significant deficiencies; and that defendants were well aware that the procedures and controls they were using to manufacture and sterilize their devices were in violation of the law; 501(a)(2)(A), 501(c), 502(a).

A consent decree of permanent injunction was entered without the defendants admitting to the truth or accuracy of any of the charges. As well as enjoining the complained of violations, the decree provided that the defendants would discontinue their medical device business, would recall any lots of devices found to be non-sterile, and would reprocess or destroy all devices in stock, all in-process devices, and all recalled devices. (Inj. 875; S. No. 78-155-106 et al.; N.J. No. 33)

Metabolic Products Inc., and **W. Leo Tew,** president, Wilmington, Dist. Del.

Charged 10-19-78 in a complaint for injunction: that the defendants had been distributing in interstate commerce tablets of amygdalin (also referred to as Laetrile and vitamin B-17), a new drug without an effective approved New Drug Application, which the defendants were dispensing without a prescription; that the drug lacked the prescription legend; that the drug lacked required label information; that the defendants were aware of the court order in *Rutherford* v. *United States* and had failed to comply with that order; that a shipment of 10,000 tablets had been detained, refused admission into the United States and been exported; 505(a), 503(b)(1), 503(b)(4), 502(f)(1).

The defendants requested the production of a number of documents, including "all documents of every kind and description relating to the subject matter of the Complaint for Injunction." The government objected to the defendants' request. The government served and the defendants answered written interrogatories. The defendants served written interrogatories on the government. After hearing testimony and receiving evidence, the court issued a preliminary injunction against the defendant firm. Subsequently, a temporary restraining order enjoined the individual until such time as the court could rule on a government motion for preliminary injunction against the individual. Thereafter, pursuant to stipulation, the action was stayed until 30 days after the decision of the Supreme Court in *United States* v. *Rutherford* No. 78-605 and/or *Rutherford* v. *United States* No. 78-763.

A preliminary injunction was issued against the defendants and was followed by a consent decree of permanent injunction. (Inj. No. 869; S. No. 78-144-686 et al.; N.J. No. 34)

NOTICE OF JUDGMENT on Miscellaneous Action

Moisturizer for skin (NMC-12) and FDA refusal to recognize such cosmetic ingredient formulation as a trade secret or as confidential commercial information, Washington, D.C.

Charged 7-26-76 by Faberge Inc., a cosmetic producer and distributor, New York, N.Y., against the FDA Commissioner Alexander M. Schmidt, FDA Assistant Commissioner John T. Walden, the H.E.W. Department, and H.E.W. Secretary F. David Mathews, in a suit for injunction, declaratory judgment and judicial review: that, after years of time-consuming, expensive research and testing, Faberge discovered and developed a cosmetic ingredient formulation code-named NMC-12; that NMC-12 was a unique, highly confidential formulation of ingredients which was not known to any of Faberge's competitors, suppliers or customers; that Faberge had taken exhaustive, expensive security precautions to preserve the secrecy of NMC-12; that the effectiveness of NMC-12 in moisturizing human skin was of significant commercial value to Faberge; that the composition of NMC-12 was not readily ascertainable by biochemical or other analytical means, but the disclosure of its ingredients would enable competitors to duplicate NMC-12; that requiring the disclosure of NMC-12 ingredients would deprive Faberge of a significant competitive advantage and would result in irreparable commercial injury to Faberge; that, pursuant to FDA regulations, Faberge had submitted confidential records and other materials pertaining to the formulation of NMC-12 to FDA and had requested FDA to declare NMC-12 a trade secret and/or confidential commercial information; that FDA had denied Faberge's request, had informed Faberge that NMC-12 would not be considered a trade secret and/or confidential commercial information and had also informed Faberge that the ingredients of NMC-12 must be disclosed on its product labels; that Faberge had exhausted its administrative remedies; that such refusal to recognize NMC-12 as a trade secret and/or confidential commercial information was arbitrary, capricious, an abuse of discretion, and contrary to law; that such threatened disclosure of NMC-12 was in excess of statutory jurisdiction, was in derogation of 18 U.S.C. 1905 and FDA regulations, and constituted a taking of property without due process of law and without just compensation; and that the court should grant Faberge the requested judgment and injunction.

The government opposed Faberge's complaint, and served a request for the production of documents upon Faberge. Faberge objected to producing documents until after a protective order had been obtained; Faberge served written interrogatories on the government. A protective order was entered and Faberge made production of a number of documents. The government served written interrogatories on Faberge. Faberge filed a request for the production of documents. The government moved to dismiss Faberge's charges that FDA's refusal to recognize the secret/confidential nature of NMC-12 constituted taking of property without due process of law and without just compensation. The court denied such motion to dismiss on the ground that the government had not presented evidence sufficient to overcome the presumption of sufficiency of the complaint; the government moved for reconsideration.

Ultimately, pursuant to stipulation, the parties agreed: that Faberge should comply with the FDA regulations requiring disclosure of the NMC-12 ingredients when used in a cosmetic product; that FDA would not act against Faberge for prior failure to disclose the NMC-12 ingredients; and that the action was dismissed with prejudice to any claim that NMC-12 in a cosmetic constituted a trade secret or confidential commercial information. (Misc. No. 344; N.J. No. 35)

Notices of Judgment are given pursuant to section 705 of the Federal Food, Drug, and Cosmetic Act. Notices of Judgment report cases involving seizure proceedings, criminal proceedings, and injunction proceedings. Seizure proceedings are civil actions taken against *goods* alleged to be in violation, and criminal and injunction proceedings are against *firms* or *individuals* charged to be responsible for violations. The cases generally involve foods, drugs, devices, or cosmetics which were alleged to be adulterated or misbranded or otherwise violative of the law when introduced into and while in interstate commerce, or while held for sale after shipment in interstate commerce.

Notices of Judgment are prepared by Food and Drug Division, Office of the General Counsel, HHS.

Published by direction of the Secretary of Health and Human Services.

Arthur Hull Hayes Jr., M.D., *Commissioner of Food and Drugs*
Washington, D.C., June 1, 1982

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Section 705[375] of the Food, Drug, and Cosmetic Act: (a) The Secretary shall cause to be published from time to time reports summarizing all judgments, decrees, and court orders which have been rendered under this Act, including the nature of charge and the disposition thereof.
(b) The Secretary may also cause to be disseminated information regarding food, drugs, devices, or cosmetics in situations involving, in the opinion of the Secretary, imminent danger to health, or gross deception of the consumer. Nothing in this section shall be construed to prohibit the Secretary from collecting, reporting, and illustrating the results of the investigations of the Department.

☆U.S. GOVERNMENT PRINTING OFFICE 1982—361-174/116

How Healthy Is

1. **What is America's most popular drug?**
2. **Is glaucoma hereditary?**
3. **Is there a cure for baldness?**
4. **Can sleeping pills interfere with your sleep?**
5. **Are natural vitamins better than synthetic ones?**
6. **True or false: The FDA proposed in 1977 to ban saccharin.**
7. **Is sugar consumption in the United States going up or down on a per capita basis?**
8. **Do some food additives serve only a cosmetic purpose?**

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Answers to quiz: 1. Excluding alcohol, aspirin is America's most popular drug. 2. Some but not all glaucoma is hereditary. 3. There is no cure for baldness. 4. Sleeping pills, if taken over an extended period, may interfere with regular sleeping patterns. 5. Natural and synthetic vitamins are virtually the same. 6. False. FDA's proposal was for a *partial* ban. 7. Refined sugar consumption is going down, but consumption of sugar from other sweeteners—mainly from corn syrup—is going up, leading to an overall increase. 8. Some food additives serve to make food look more natural and thus more appetizing.

Your Health IQ?

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FDA CONSUMER

Who, Why, When And Where Of Food Poisons

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Using the Store Shelf as a Food Label 22
Markers showing products low in sodium, calories and fat make it easier for dieters to locate the right packages.

Who, Why, When and Where of Food Poisons (And What To Do About Them) 24
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A new way of shopping saves time for persons on special diets and permits them to get better control over what they eat. Such placards as the one shown at left are placed near foods that are low in sodium, cholesterol and fat, or calories to point them out to the dieter. For an account of testing of this new system, see Using the Store Shelf as a Food Label, *page 22.*

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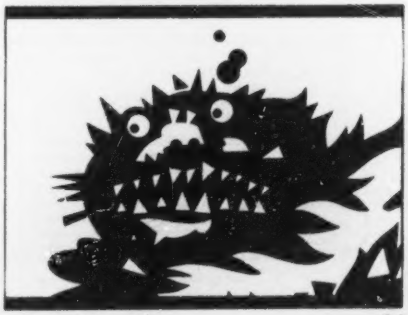

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Drug Leaflets Provided

Members of the American Association of Retired Persons and National Retired Teachers Association will be receiving easy-to-understand drug information leaflets with their prescriptions in a new program sponsored by the NRTA/AARP Pharmacy Service. The program, announced May 4, is the first of its kind for any age group.

The leaflets, prepared with the assistance and cooperation of FDA and experts in geriatric medicine and pharmacy, represent the first national voluntary effort by any private or government organization to provide written drug information to consumers at the time prescriptions are filled.

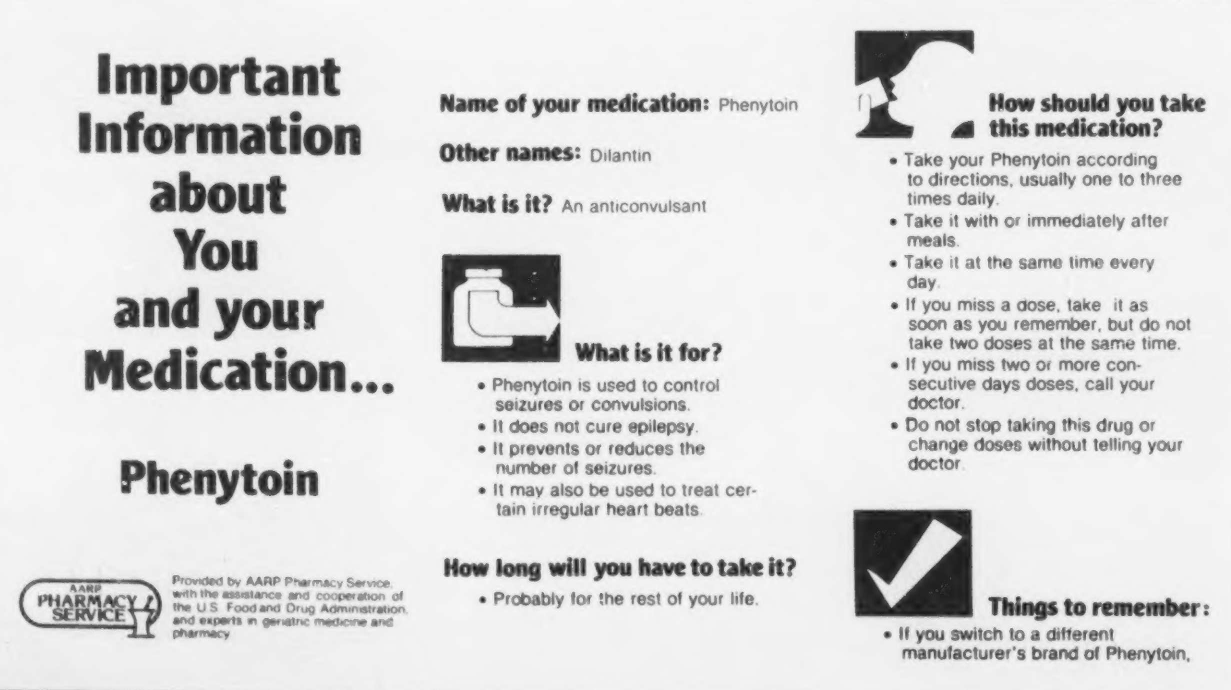
Each leaflet instructs the consumer how to take the drug, provides important facts to remember, describes the drug's uses and possible side effects, and explains what information the doctor needs to know when prescribing it.

The leaflets are being prepared for drugs most often consumed by older persons and will be made available to association members at no charge when their prescriptions are initially filled by their pharmacy service. Five leaflets are now available: for the heart drug digoxin, the diuretic (or water pill) furosemide, the anti-convulsant phenytoin, the high blood pressure medicine Aldactazide, and the cholesterol-lowering drug clofibrate. Thirty-five more leaflets are planned.

Persons over age 65 consume one-fourth of all prescriptions filled in the United States and, as a group, are more prone to side effects from drug therapy than are younger persons.

The nonprofit NRTA/AARP Pharmacy Service provides prescription drugs and other health care items to the 13 million members of the two retiree organizations. It is the world's largest private mail service pharmacy, filling more than 4.5 million prescriptions a year.

Reproduced below is one of the six-page leaflets reduced in size by one-third.



Important Information about You and your Medication...

Phenytoin

AARP PHARMACY SERVICE

Provided by AARP Pharmacy Service with the assistance and cooperation of the U.S. Food and Drug Administration, and experts in geriatric medicine and pharmacy

Name of your medication: Phenytoin

Other names: Dilantin

What is it? An anticonvulsant

What is it for?

- Phenytoin is used to control seizures or convulsions.
- It does not cure epilepsy.
- It prevents or reduces the number of seizures.
- It may also be used to treat certain irregular heart beats.

How long will you have to take it?

- Probably for the rest of your life.

How should you take this medication?

- Take your Phenytoin according to directions, usually one to three times daily.
- Take it with or immediately after meals.
- Take it at the same time every day.
- If you miss a dose, take it as soon as you remember, but do not take two doses at the same time.
- If you miss two or more consecutive days doses, call your doctor.
- Do not stop taking this drug or change doses without telling your doctor.

Things to remember:

- If you switch to a different manufacturer's brand of Phenytoin,

Acne Drug Approved

FDA has approved a new prescription drug capsule for the treatment of cystic acne, the most severe and disfiguring form of acne. The United States is the first nation to approve this important new drug, which will be marketed by Hoffmann-La Roche Inc. under the brand name Accutane.

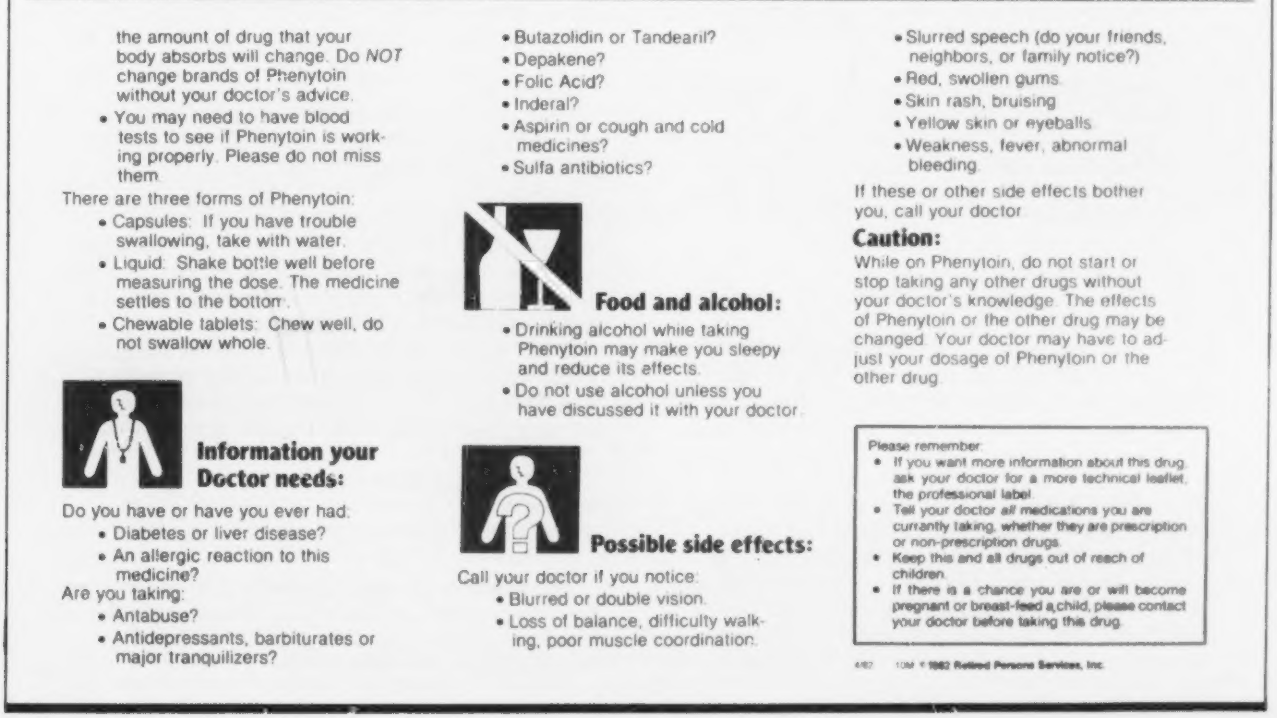
The drug, 13-cis retinoic acid, also known chemically as isotretinoin, is a derivative of vitamin A. However, the vitamin itself is not of established value in treating acne and may be toxic in large doses. Accutane is intended for use in treating cases of severe, recalcitrant cystic acne that have been unresponsive to any other therapy such as antibiotics. It is not intended for use in treating common, uncomplicated cases of acne.

Far worse than the typical acne that comes and goes in the teen years, cystic acne is a chronic disorder of the oil glands primarily involving the face, neck and back. In most cases, cystic acne causes deep pitting and scarring. About 350,000 people in the United States suffer from this disease.

The exact mechanism of Accutane's action is unknown. The most recent evidence, however, suggests that it reduces the size of oil glands, decreasing their production of fatty material. Treatment requires eight weeks, followed by another eight weeks, if necessary, after a rest of a similar period. In studies of the drug, treatment resulted in complete and prolonged remission from the disease in most patients.

A Limit to Lasers

Lasers have a variety of uses ranging from colorful displays that entertain to delicate surgery to repair damaged eyes (see "Entertainment Lasers: Approach With Care," *FDA Consumer*, September



the amount of drug that your body absorbs will change. Do *NOT* change brands of Phenytoin without your doctor's advice.
- You may need to have blood tests to see if Phenytoin is working properly. Please do not miss them.

There are three forms of Phenytoin:
- Capsules: If you have trouble swallowing, take with water.
- Liquid: Shake bottle well before measuring the dose. The medicine settles to the bottom.
- Chewable tablets: Chew well, do not swallow whole.

Information your Doctor needs:

Do you have or have you ever had:
- Diabetes or liver disease?
- An allergic reaction to this medicine?

Are you taking:
- Antabuse?
- Antidepressants, barbiturates or major tranquilizers?
- Butazolidin or Tandearil?
- Depakene?
- Folic Acid?
- Inderal?
- Aspirin or cough and cold medicines?
- Sulfa antibiotics?

Food and alcohol:
- Drinking alcohol while taking Phenytoin may make you sleepy and reduce its effects.
- Do not use alcohol unless you have discussed it with your doctor.

Possible side effects:

Call your doctor if you notice:
- Blurred or double vision.
- Loss of balance, difficulty walking, poor muscle coordination.
- Slurred speech (do your friends, neighbors, or family notice?)
- Red, swollen gums.
- Skin rash, bruising.
- Yellow skin or eyeballs.
- Weakness, fever, abnormal bleeding.

If these or other side effects bother you, call your doctor.

Caution:

While on Phenytoin, do not start or stop taking any other drugs without your doctor's knowledge. The effects of Phenytoin or the other drug may be changed. Your doctor may have to adjust your dosage of Phenytoin or the other drug.

Please remember:
- If you want more information about this drug, ask your doctor for a more technical leaflet, the professional label.
- Tell your doctor *all* medications you are currantly taking, whether they are prescription or non-prescription drugs.
- Keep this and all drugs out of reach of children.
- If there is a chance you are or will become pregnant or breast-feed a child, please contact your doctor before taking this drug.

4/82 10M © 1982 Retired Persons Services, Inc.

1978). The newest wrinkle in the laser field involves the use of laser beams for face-lifts, acupuncture and other non-surgical therapeutic procedures. These treatments are sometimes described in advertisements as "biostimulation."

In "laser acupuncture," the practitioner applies a low-power laser beam instead of needles to traditional acupuncture points, purportedly for relief of pain or other therapeutic purposes. In "non-surgical face-lifts," the laser beam is directed at certain points (acupuncture points) on the face or is scanned across the entire part of the face to be treated. The treatment is often accompanied by electrical stimulation, vitamin therapy and cosmetics.

Although high-power lasers are of proven benefit in many surgical procedures, such as eye surgery, FDA has not approved the use of any laser for non-surgical therapeutic procedures. Laser devices intended for these uses are therefore considered investigational and may be used on humans only under the terms of an investigational device exemption.

The exemption requires review and approval of an investigational protocol by an institutional review board (and by FDA if the investigation involves significant risk or the device is inherently dangerous). The device also must be labeled as investigational and patients must give their consent in writing to be subjects in a clinical trial.

The manufacturer may not promote the investigational laser devices as safe and effective but may solicit investigators and provide the devices to them. Practitioners who use the devices should limit such use to investigation in approved clinical trials. They, too, are prohibited from promoting the procedures as safe and effective. Such promotion would make the device misbranded under the law.

The Bureau of Radiological Health has asked the national chiropractic associations to inform their members of the investigational status of laser devices for non-surgical therapeutic uses. Articles to that effect have been published in chiropractic journals.

The bureau also has informed the two principal manufacturers of lasers intended for these purposes of the agency's position. The manufacturers are Dynatronics Research Corp., Salt Lake City, which manufactures the Dynatron 820 laser, and Omni International, Topeka, Kan., which manufactures the Omni Probe 1000. The two have agreed to label the devices as investigational and distribute them in accordance with the investigational device exemption regulations. Clinical trials are to begin soon.

Infant Formula Rules

FDA's final regulations governing the recall of defective infant formulas went into effect June 1. The new rules, mandated by the Infant Formula Act of 1980, are intended to ensure that recalls are effective and complete and to improve FDA's ability to monitor the recalls more effectively.

The final version of the infant formula recall regulations was published in the April 30 *Federal Register*. Regulations establishing quality control procedures manufacturers must follow, also mandated by the Infant Formula Act, were published earlier.

Consumer Forum

Steel for Lining Pots

As a long time manufacturer and marketer of high quality cookware, we enjoyed your article on "Cookware as a Source of Additives" [*FDA Consumer*, March 1982].

Revere Ware basically produces stainless steel and copper cookware and lines all its copper ware with 304 stainless.

Your recommendation that consumers use only tin lined copper cooking utensils may have overlooked or not known of the existence of stainless lined copper.

We have used hygienic, top grade stainless for many years. We certainly hope your recommendation does not exclude stainless as it is superior to tin in all respects and so much more durable. Unlined copper is definitely not recommended.

If you agree with the safety of stainless lining, I would appreciate a small article to that effect so no possible injury could occur by anyone misconstruing stainless steel's omission as a negative . . . .

J. M. Eikenberg, President
Revere Ware
Clinton, Ill.

Mr. Eikenberg is right. Stainless steel can be used for lining copper cookware; it is considered both safe and durable. The metal should have been included as an alternative to tin.

The Notebook

The Notebook: a potpourri of items of interest gathered from FDA news releases, other news sources and the Federal Register *(designated* FR, *with date of publication). The* Federal Register *is available in many large public libraries.*

■ FDA has formally announced its proposal to exempt all classes of **antibiotic drugs** from batch certification requirements. The exemption also applies to susceptibility devices used to select the appropriate antibiotic for specific treatment. The agency's decision was based on the high level of manufacturer compliance with existing standards (*FR* May 7).

■ Until physicians can say with assurance that **ultrasound** does not produce subtle or delayed harmful effects, it should be used only when medically necessary and not routinely for all pregnancies. These conclusions came out of a symposium held by Columbia University College of Physicians and Surgeons and the March of Dimes Birth Defects Foundation. They were reported in the April 23/30 *Journal of the American Medical Association.*

■ **Bone meal and dolomite,** sometimes used as calcium supplements, should be used as little as possible in infants, young children, and pregnant or lactating women, FDA says in the April *Drug Bulletin.* Agency scientists have found high levels of lead in samples of both substances. Ingested excessively, lead may produce toxic reactions, including central nervous system damage, anemia and abdominal pain.

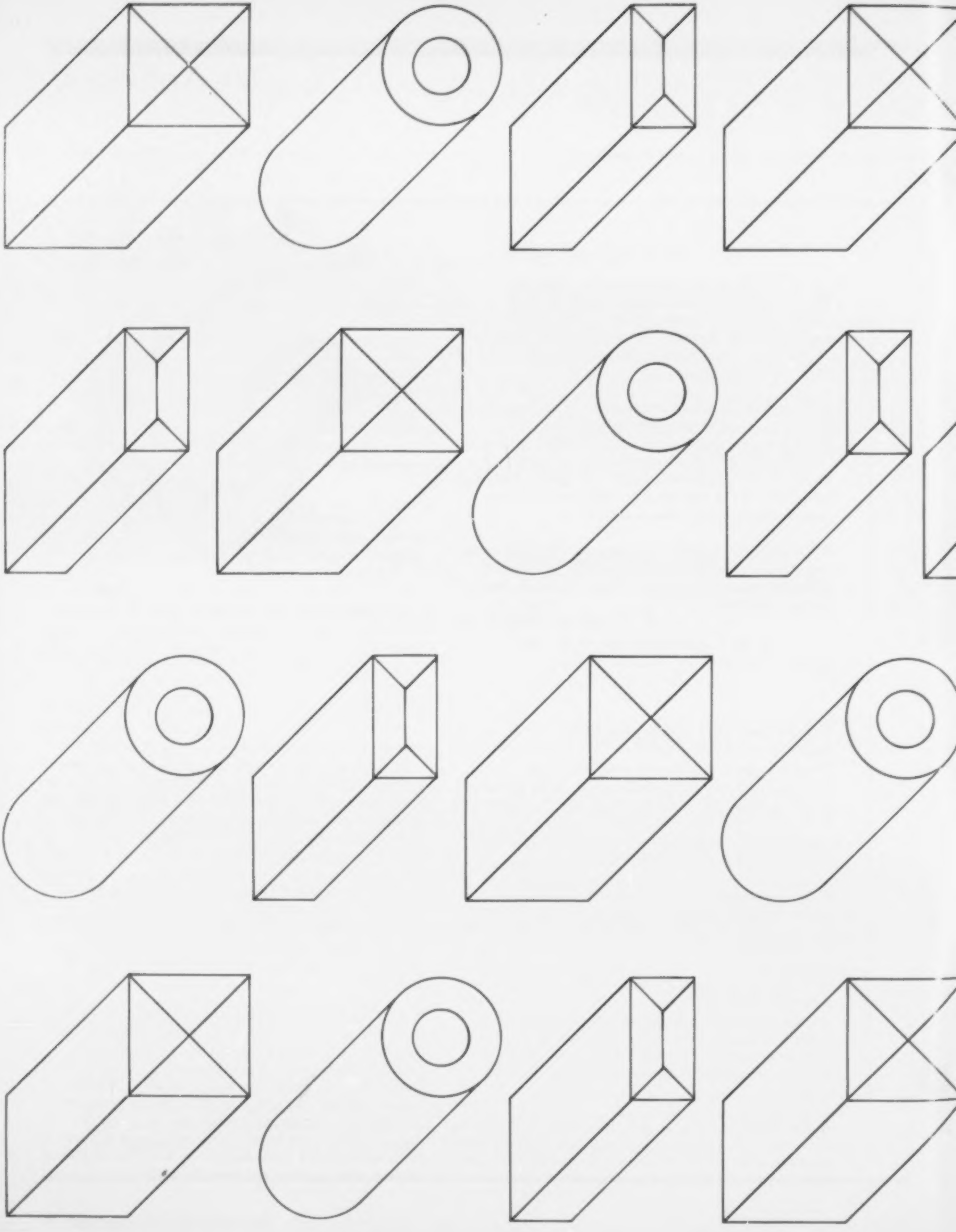
■ To save money, many American hospitals are limiting the number of drugs stocked in their pharmacies and are dispensing **therapeutic alternatives,** according to a nationwide survey conducted by University of Florida researchers. Of the 2,437 hospitals responding, 31 percent said they allow pharmacies to stock and substitute one drug from a category of specific drugs originally prescribed by physicians. This practice is called therapeutic substitution. With generic substitution the drug must be "chemically" equivalent. One brand is substituted for another brand of the same drug.

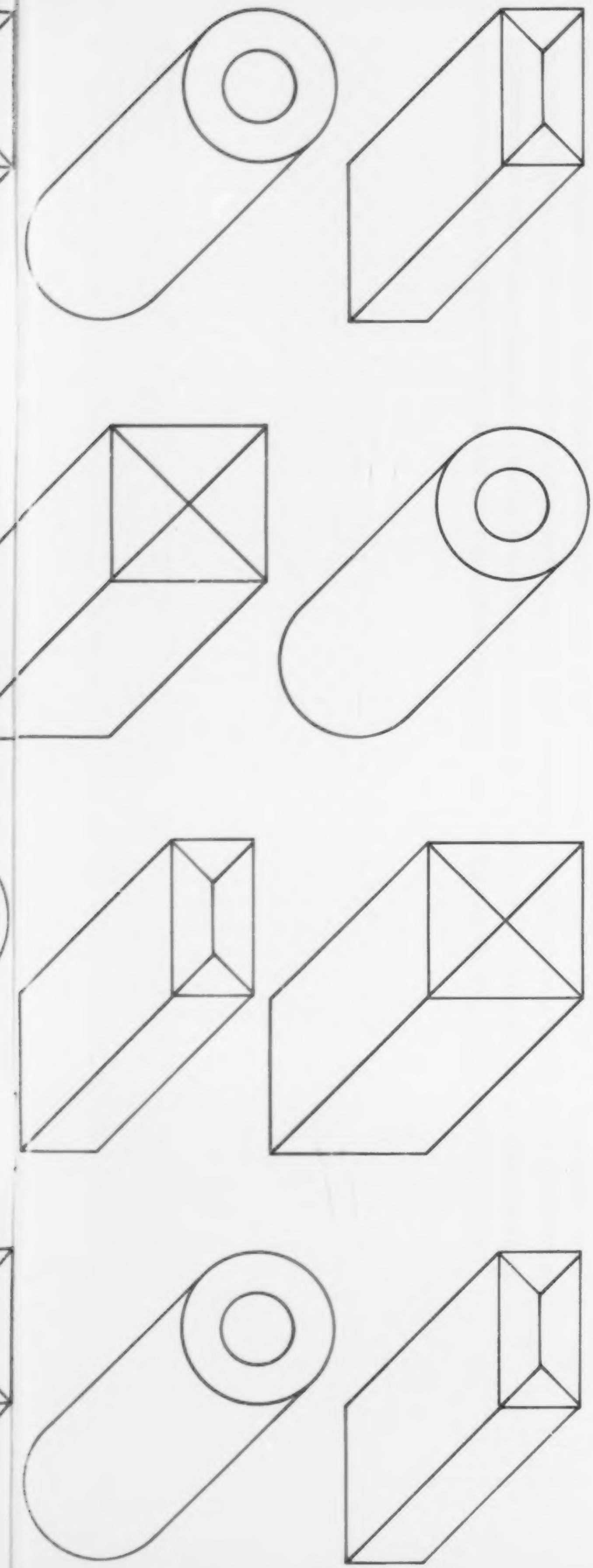
■ Enforcement rules for OTC (over-the-counter) drugs have been changed to allow the antihistamine **diphenhydramine** to be sold in non-prescription nighttime sleep aids. The switch from prescription only to non-prescription status, recommended by an OTC review panel, was made by FDA after two manufacturers provided evidence of the drug's safety and effectiveness as a sleep aid (*FR* April 23).

■ The Nuclear Regulatory Commission has proposed to amend its regulations covering **teletherapy:** radiation treatment by massive doses administered at a distance from the body. The amendments would require installation of radiation monitors in teletherapy rooms; use of portable survey instruments when monitors fail; and inspection and servicing of machines during replacement of the radiation source or at intervals not to exceed five years, whichever comes first (*FR* April 28).

■ FDA has called for comments regarding potential for abuse, actual abuse and medical usefulness of 15 **benzodiazepine drugs.** The World Health Organization will use this information in considering whether to recommend international restrictions on these drugs (*FR* May 7).

■ RECALLS: **Exercise bicycles** distributed by Beacon Enterprises Inc., Yonkers, N.Y., were recalled in April. At least 15 people were injured when the metal seat support post broke through the seat. . . . Robertson Resources Ltd., Salisbury, Md., recalled its **Revital** powder and gel, non-prescription products promoted for treatment of acne, skin ulcers, herpes, surgical wounds and serious burns. FDA tests found the products were heavily contaminated by bacteria capable of causing serious injury and possibly death.





Old Milk Stays Fresh In Aseptic Package

by Chris Lecos

Displayed prominently in the advertisement that appeared recently in a Houston, Texas, newspaper was a rectangular-shaped, flat-topped carton of low-fat milk. That in itself was not unusual. But what may have caught the eye and piqued the curiosity of food shoppers there was what the ad said:

> **Week after week after week it stays fresh and delicious—with or without refrigeration!**
>
> **Here's the milk you can buy now and drink later—weeks and months later if you wish! It comes in an extraordinary new carton made possible by advanced technology, so you can keep it in a cupboard or keep it in a refrigerator . . . You just refrigerate after opening.**

The store selling the milk did not have to stock it in a refrigerated area. A shopper could take it home and store it at room temperature until it was to be consumed, perhaps several months later—maybe as much as six months.

During the next few years American consumers can expect to be barraged by a growing number of specially packaged products whose long shelf life and stability will be extolled by the companies that produce them. Various milk and juice type beverages are expected to dominate the new flexible package choices but, according to trade press reports, an expanded array of other products also may start hitting the marketplace.

The "advanced technology" referred to in the Houston ad deals with the way the food container is chemically sterilized for safe storage. The process is known as aseptic processing and packaging. The term is probably foreign to most shoppers although the technology itself is by no means new. In Europe and other parts of the world aseptically processed and packaged milks, juices, fruit juices and other product choices have been marketed for more than 20 years.

The U.S. industry's interest, according to various trade press reports, has surged in recent years, primarily because of a food additive regulation published by the Food and Drug Administration on Jan. 9, 1981. In effect, FDA gave the food industry a green light to use hydrogen peroxide to sterilize polyethylene food-contact surfaces. Polyethylene is a plastic material that can be used to line a flexible food carton. FDA said hydrogen peroxide is safe to use under prescribed conditions for such cartons. Food that comes into contact with the chemically sterilized polyethylene can be consumed safely, FDA said.

The agency had been told in early 1980 of a Hiroshima University mouse study that suggested hydrogen peroxide might cause cancer in the duodenum, a portion of the small intestine. The agency then decided to review all safety data on hydrogen peroxide, including the Hiroshima study. Upon completion of the review, FDA said that there was insufficient evidence from the Japanese study and elsewhere to conclude that hydrogen peroxide is a duodenal carcinogen. FDA also said the potential level of migration of hydrogen peroxide into a food product would not be harmful to public health. In the sterilization of any food packaging material, FDA said, the residue level in the food immediately after packaging must not exceed 0.1 parts per million—or the equivalent of 100 parts per billion. This level was established on the basis that the hydrogen peroxide residue would dissipate to 1 part per billion or less within 24 hours from the time a product is packaged.

FDA's action ensued from a petition filed with the agency in September 1979 by Brik Pak Inc., a Dallas aseptic packaging firm. Brik Pak had been formed in 1977 by Tetra Pak International, which is based in Lund, Sweden, and which first introduced its aseptic processing and packaging system for liquid foods in Europe in 1961. Tetra Pak has been using hydrogen peroxide as a chemical sterilant in its operations. More than 15 billion units were produced last year in more than 70 countries around the world, the company said.

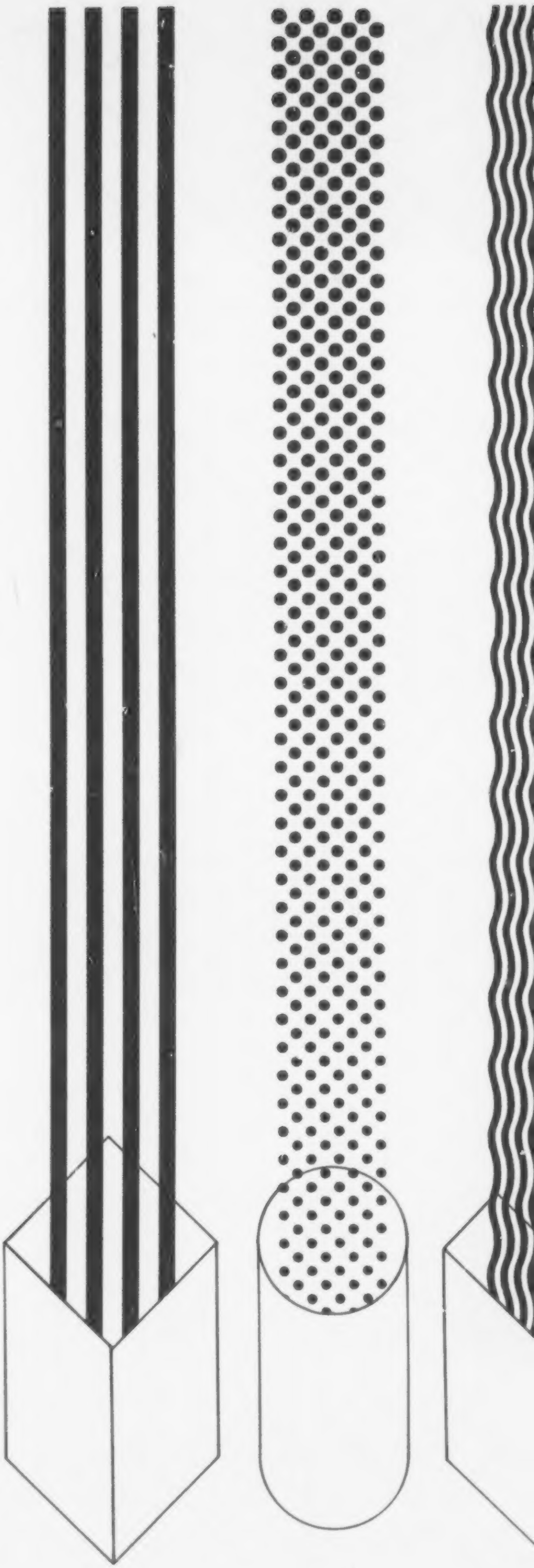
Just what is aseptic packaging and how does it differ from packaging a product in a metal can, a glass jar or a plastic pouch?

The dictionary says aseptic means free of disease-producing or putrefying microorganisms. One of FDA's major tasks is to assure that the amount of any chemical that may migrate and become an additive in a food will not be harmful to eat. In this instance FDA had to amend its food additive regulations because hydrogen peroxide can migrate into food as an indirect additive.

Sterility—a state in which all microorganisms that can spoil a food have been totally destroyed—is not sought in every packaging process. An effective packaging system's goal is to achieve "commercial sterility," as defined in the *Code of Federal Regulations.* A commercially sterile food is one that has been processed to a point where it is free of microorganisms that could harm public health or which might cause a non-refrigerated food to spoil during storage and distribution.

Aseptically processed milk, which is a low-acid food, is raw fluid milk that has been commercially sterilized at high temperatures, then slightly cooled and poured into a polyethylene-lined container sterilized with hydrogen peroxide. The container is sealed, allowing no air to enter. Even when stored at room temperatures, the milk has a much longer shelf life than its refrigerated counterpart.

Most non-acid canned foods, such as corn or peas, are



not sterilized when first put into a can, glass container or plastic pouch. They are made safe to eat (and cooked in the process) as a result of thermal (heat) processing after the foods have been hermetically sealed—that is, packaged in a container that's airtight.

According to FDA packaging experts, there is no practical technique at the present time for the aseptic processing of solid foods in flexible type packages.

When food is aseptically processed and packaged, the food and the package are sterilized separately. The mechanical process that brings the food and package together must also provide sterile conditions. What happens, in effect, is that the food is heated for the required length of time and then cooled; the container is exposed to a hydrogen peroxide solution in a separate operation; and the container is filled with food and sealed in a commercially sterile environment.

Foods can be aseptically packaged without using chemicals in or on the packages. In 1949, for example, an aseptically canned split pea soup was sold in the United States. In the 1960s, snack packs of milk puddings in aluminum cans were marketed successfully as lunch box desserts. They are still being sold today. So, in that sense, aseptic packaging is not new even to Americans.

However, aseptic packaging in plastic and plastic-coated paper containers is much more complicated than aseptic packaging in a metal container, especially since it is not possible to thermally treat plastics at the higher temperatures that can be used with cans. FDA's consent for use of hydrogen peroxide on polyethylene containers has led to a food industry search for items that may be packaged at less cost than is required for conventional metal or glass. The rising costs of energy were also cited as a principal reason for current industry interest in aseptic processing for flexible packages.

Some major companies already have voiced a strong interest in aseptic packaging, including Ocean Spray, Borden, General Foods, Coca-Cola and Del Monte. Dairymen Inc., an 8,000-member cooperative of dairy farmers in 17 Eastern and Southeastern states, has built a $14-million plant in Savannah, Ga. There the firm hopes to produce 80,000 gallons of aseptically packaged milk each day. Whole, low-fat and flavored milks reportedly are to be produced there. Some dairy industry spokesmen believe that the new flavored milks could compete with soft drinks.

"There is tremendous interest out there and becoming more so all the time," said Cleve Denny, director of research for the National Food Processors Association in Washington, D.C. When the Food and Dairy Expo was held in Atlanta last November, five major companies introduced aseptic packaging systems. When the same event took place in Chicago two years earlier, only Brik Pak exhibited.

No one currently sees aseptic packages replacing cans and glass. The principal markets for aseptic containers include the vending machine industry, the recreation market (campers, hunters, etc.), the shipping industry, the military, small retail outlets that lack storage and refrigeration space, and working couples who don't have much time to shop for food.

There are literally hundreds of new product opportunities in various segments of the consumer market, according to Alden Grimes, executive vice president of the American Dairy Association, as reported in *Food Engineering* magazine. "Special milks for the lactose intolerant, the baby formula market and such milk-based products as salad dressings, cream or white sauces, etc., are only a few ways in which the total demand for milk could be expanded," he said.

Prior to approval, FDA had taken the position that the food industry had to demonstrate with acceptable scientific evidence that the use of chemical sterilization of aseptic packaging containers is safe. FDA detailed its position on hydrogen peroxide sterilization for aseptic processing and packaging in a paper presented last November to New England food and drug officials. The paper was written by Rees B. Davis, currently assistant director for packaging technology, and Dennis M. Dignan, a food technologist in FDA's plant and protein technology branch.

"Hydrogen peroxide sterilization is a new technology—a new frontier in food processing that has been encouraged by recent (FDA) regulation," the paper noted. "It is essential for safety that industry assure good manufacturing practices in its use."

The authors said that users of hydrogen peroxide sterilization and also food and drug enforcement officials must recognize that use of this technology requires adherence to FDA's food additive regulations.

After FDA allowed the use of hydrogen peroxide for polyethylene surfaces, the National Food Processors Association asked the agency whether other types of packaging materials could also be used. FDA replied that it anticipates no problems with the use of the chemical as a sterilant on inert surfaces such as glass or metals that are uncoated as long as industry complies with regulations. FDA also indicated that composite cans lined on the inside with polyethylene are acceptable.

However, certain types of other plastic coatings used on packaging materials, but which are not covered by the regulation, would have to be tested before FDA would permit their use with hydrogen peroxide. The regulation does not permit coatings other than polyethylene. More information is needed on other polymeric food contact surfaces to determine whether sterilization with hydrogen peroxide will significantly alter the extractives migrating to food. Until more is known, the present number of possible package materials for hydrogen peroxide sterilization will be somewhat limited.

Chris Lecos is a member of FDA's public affairs staff.

How The Measles Virus Was Done In

by Judith Willis

The shades were drawn against the bright sunlight that bothered the child's eyes. Brass bands parading by the window to celebrate the end of World War II did not cheer the little girl, who lay listlessly in her bed.

The doctor, summoned to the house for the second time in as many days, bent to examine the 4-year-old. Her rash had worsened, as had the cough. Her eyes were redder, and her fever was now 103.5 degrees despite aspirin.

The doctor turned from the child and motioned the mother to follow him out of the room. "I'm afraid there's nothing more we can do but wait it out," he said when they were out of the child's earshot. "If she gets through the next 24 hours, she'll probably be all right."

Once, this scenario was not uncommon in homes across the United States, as measles struck some 525,000 children a year. But today this childhood disease, which can have serious complications, is all but eradicated in the United States—thanks to a vaccine developed in the 1960s.

The picture was usually the same: The disease had started out like a cold. The child had a stuffy, runny nose, bleary red eyes and a cough. After about four days, during which the symptoms worsened, it would become clear that this was not a common cold. Finally, a rash would appear, making it clear that the malady was the measles.

If the child had been seen by a physician before the rash emerged, or if an adult in the family knew what to look for, the measles might have been diagnosed. An early sign was the appearance of Koplik's spots, small red spots with bluish white specks in the center, that started out inside the cheeks near the molars and then spread to the entire cheek and lip area.

The rash usually did not appear until two days after the Koplik's spots, three to four days after the child had first become ill. After the rash appeared, all symptoms, including the fever, would worsen for two to three days and the Koplik's spots would begin to fade. Then, often suddenly, the child's temperature would fall, the nasal stuffiness and conjunctivitis (red eyes) would clear and the cough improve. The rash, too, would fade.

For the majority of children, the impact of measles was over and they were left with a lifetime immunity to the disease. But a small percentage suffered complications, some not apparent until months or years later.

Middle ear infections, developing during the acute phase of the illness, were a cause for serious concern in the pre-penicillin era. Pneumonia was relatively common and frequently fatal. In some cases it was due to a bacterial infection to which the measles virus made the child more susceptible. In these cases, antibiotic treatment was usually effective. But in other children, pneumonia was caused by the virus itself and could not be treated with antibiotics.

Appendicitis, a fairly infrequent complication, was often serious enough to necessitate removal of the appendix. The infrequent complications of obstructive laryngitis and a combined inflammation of the larynx and trachea usually called for a tracheostomy, the insertion of a tube into the trachea to aid breathing.

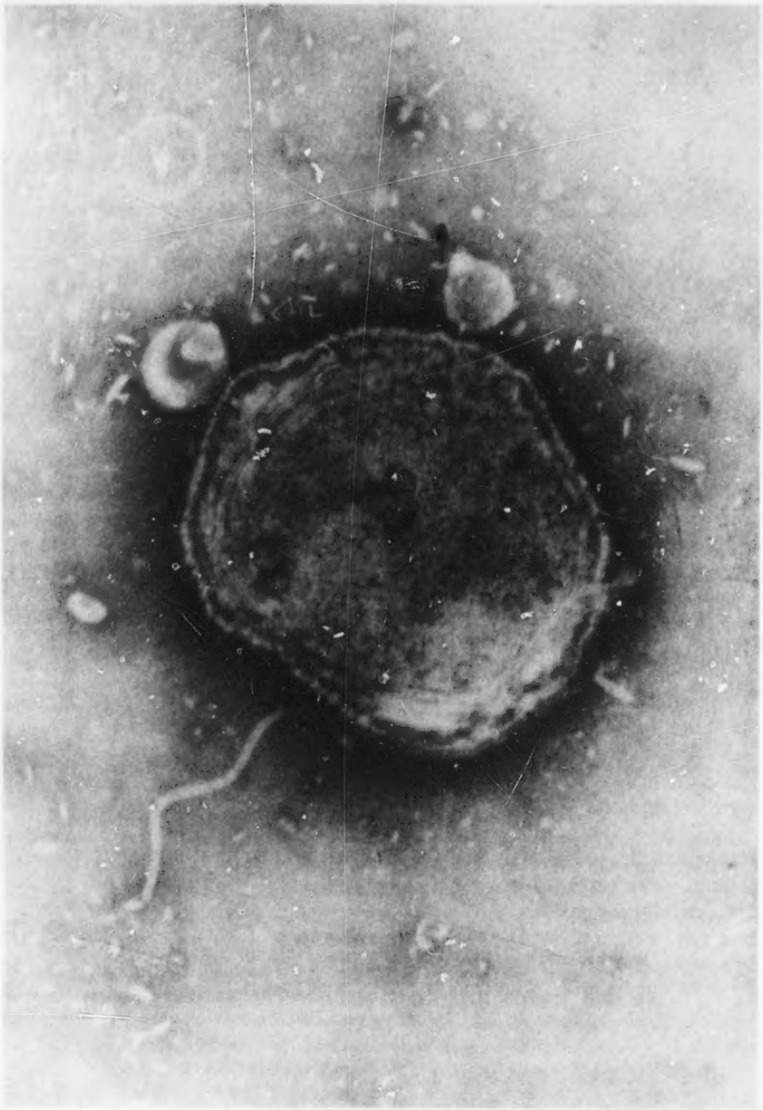
A more severe complication of measles is acute encephalitis. This potentially crippling and sometimes fatal brain disease occurred in approximately one-tenth of U.S. measles cases, usually on the second to sixth day of the rash. Although 60 percent of patients with measles encephalitis recover completely, 15 percent die, and 25 percent suffer permanent brain damage.

Another severe but more insidious complication is a disease called subacute sclerosing panencephalitis (SSPE). Its onset occurs, on the average, seven years after a measles infection, but incubation periods of several months to 15 years have been reported. SSPE is a brain disease involving behavioral and intellectual deterioration, the first signs of which may be stumbling and falling. It later progresses to seizures and increasing mental deterioration, often ending in death.

In some European countries such as England and France, and in many developing countries, measles epidemics still occur. The United States is one of several countries that have undertaken comprehensive vaccination campaigns including strict school entrance requirements. The campaigns have brought results: Figures from the U.S. Centers for Disease Control show that in 1981 the incidence of measles was reduced 99.4 percent from the 1950-62 pre-vaccine era.

Even before any licensing of measles vaccine in this country, U.S. health officials were asked to help control measles in other countries. This happened in 1960 when four African nations requested a supply of the measles vaccine. The vaccine had been successfully tested in 20,000 American children but had not yet been approved for use here. The Africans still wanted it because measles in their countries struck nearly all children and in some epidemics had a fatality rate of 15 percent. This high mortality rate was due to many factors, including malnutrition and the general health of the children, and their quick dehydration in the dry, hot weather. In addition, the age at which measles struck frequently coincided with the time of weaning.

In response to the African requests, scientists from the National Institutes of Health's Division of Biologics



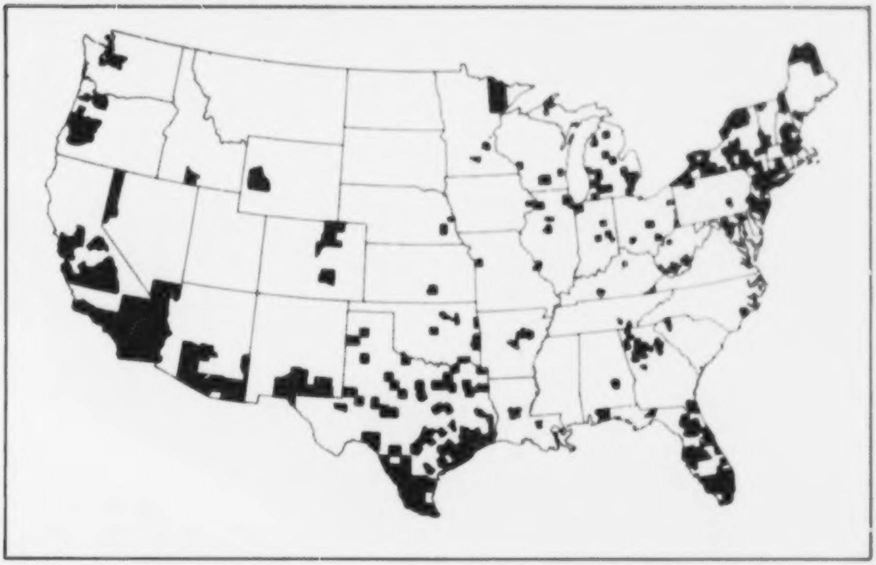
A measles virion, or single measles virus particle, magnified 75,000 times.

Standards made several trips to West Africa in the early '60s to perform clinical studies with the vaccine. These studies were essential to determine whether the vaccine was safe and effective for African children because their nutritional status and susceptibility to infection were much different from that of American children. The NIH team was headed by Dr. Harry M. Meyer Jr. (When the Division of Biologics was transferred from NIH to FDA in 1972, Meyer became its director, and he has recently been named director of FDA's Bureau of Drugs.)

The studies, involving the inoculation of native children, showed the vaccine was as safe and effective for the people of Upper Volta as it was for Americans. Ultimately, the U.S. team helped vaccinate three quarters of a million children in Upper Volta against measles. Their studies also showed that a combination vaccine, inoculating against measles, smallpox and yellow fever, was just as effective as separate injections. Subsequently, multiple vaccinations were used by the World Health Organization in its program to eradicate childhood diseases in African countries. In addition, the team found that jet injections could be safely and effectively used. This was important because it meant that the more costly and lengthy conventional techniques did not have to be used for inoculations in developing countries.

The vaccine licensed to provide immunity to measles in the United States today is the "more attenuated" live Edmonston B measles vaccine. There were two measles vaccines licensed in this country initially in 1963: the live attenuated Edmonston B vaccine and the inactivated virus vaccine. Both had drawbacks.

The live attenuated vaccine too often produced high fever as a side effect. The inactivated, or "killed," virus vaccine conferred an immunity that was too transient. In addition, those who received the killed virus vaccine and were later exposed to measles frequently developed "atypical" measles, a form of the disease involving a higher incidence of serious complications and a different type of rash than that seen with "wild" measles (the natural form). This is the only licensed killed vaccine found to have



U.S. counties reporting measles in 1981. (Two counties in Hawaii and none in Alaska reported measles.)

such side effects. (Other licensed killed vaccines include those for influenza, polio and rabies.)

The killed measles vaccine was in use in this country from 1962 to 1969. Most of the children who received it are now teen-agers, and it is this age group that suffers many of the current cases of measles. An estimated 54,000 persons in the United States received the killed vaccine and have not been revaccinated with the live. If exposure to measles is likely, those persons who have previously received the killed vaccine should be revaccinated with the live vaccine.

In the mid-1960s the "more attenuated" live Edmonston vaccine was developed. (Attenuation of vaccine refers to the weakening of the live virus.) The measles virus in this vaccine has been weakened to a point where there are far fewer reactions from the vaccine but a sufficient level of immunity is established.

Initially, infants were inoculated when they were 6 months old, but it was discovered that the carry-over of maternal antibodies reduced the effectiveness of the vaccine. If a mother has had measles before becoming pregnant, she carries antibodies to the virus. During pregnancy, antibodies cross the placental barrier and go into the bloodstream of the child. They are present at birth and remain or "persist," in the child's system, providing protection for several months after birth.

If children are inoculated against measles when they still have high levels of maternal antibodies, the vaccine will not be effective. Earlier studies had mistakenly suggested that these maternal antibodies persisted in infants up to 6 months of age, and occasionally, in very low amounts, up to 11 months of age. Therefore, the age for measles vaccination was set for 12 months, and in the face of a community outbreak could be lowered to between 6 to 12 months of age. However, it was found that only 80 to 85 percent of children immunized against measles at 12 months of age were protected against the disease. FDA scientists suspected that even at 12 months children may have enough maternal measles antibodies to interfere with immunization and that their presence was undetected because of the insensitivity of tests used at that time.

Their suspicion was confirmed when an FDA scientist, Dr. Paul Albrecht, developed a more sensitive test that could detect maternal antibodies as long as they persisted. As a result, the time of vaccination was changed to after the first birthday, preferably after 15 months of age. The new test was used to monitor immunity following inoculation with the more attenuated live vaccine. Without it a high failure rate in children vaccinated before they were a year old might have been mistakenly attributed to excessive attenuation of the vaccine rather than to the actual cause of the failures, the persistence of maternal antibodies.

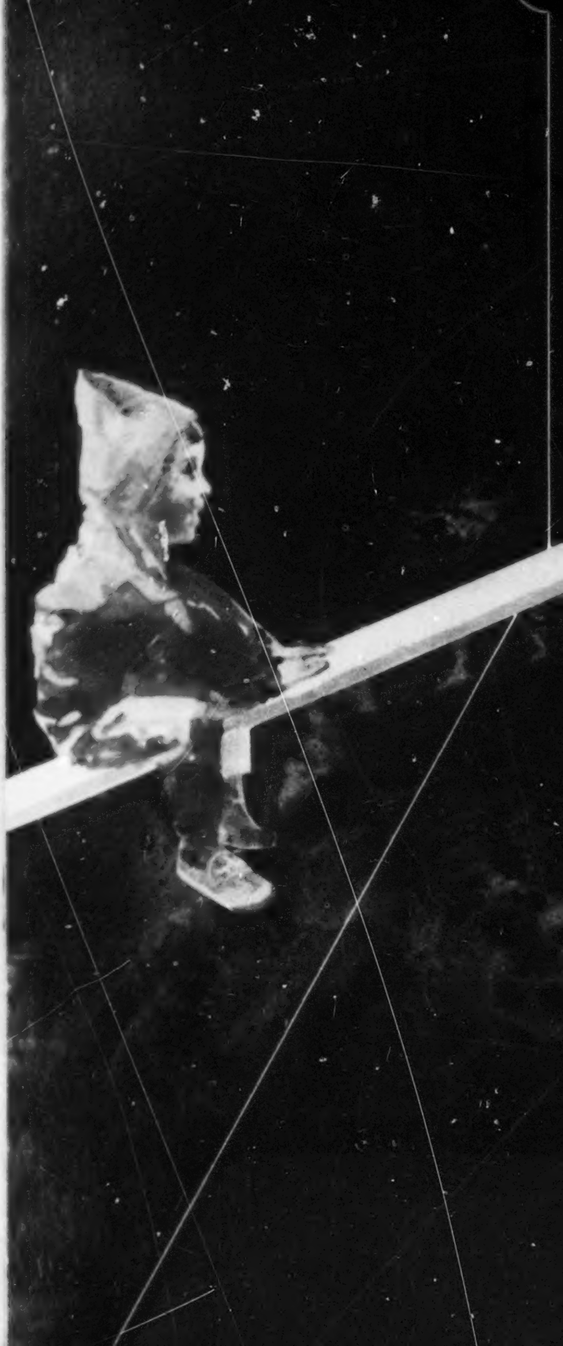
After the licensing of the more attenuated live measles vaccine, vaccination became more common in the United States. Most private physicians recommended it, and many localities required it for school entrance. By the mid-1970s this country had included measles in its nationwide childhood immunization program. In 1978, the Department of Health, Education, and Welfare announced a new "initiative" to eliminate measles from the United States by Oct. 1, 1982. It now looks as though this target date will be met.

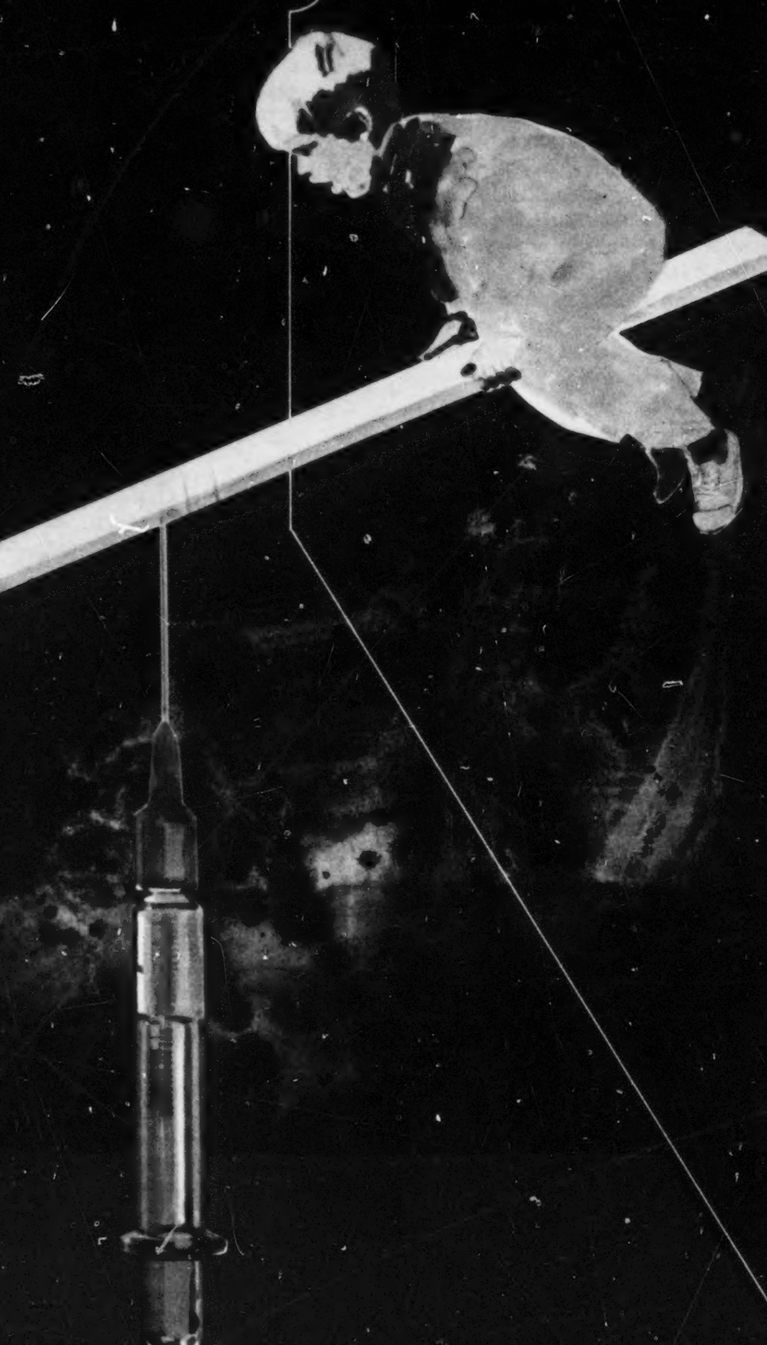
Thanks to school entrance rules requiring vaccinations, the number of reported measles cases in the United States dropped to a record low in 1981, a total of 3,032 cases.

Ninety percent of the nation's counties reported no measles in 1981, and only 1.7 percent of U.S. counties reported measles during five or more weeks, according to the Centers for Disease Control. More than half the states reported fewer than 10 cases of measles in 1981. Eight states had none—Alaska, Delaware, Mississippi, Montana, North Dakota, Rhode Island, South Dakota and Utah. In five reporting areas (Alabama, the District of Columbia, Idaho, Iowa and Vermont) all cases were foreign importations or could be linked to those importations.

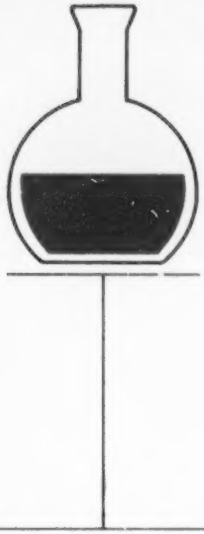
The eradication of measles in this country, however, will not mean the end of scientific interest in this disease. On the contrary, scientists continue to have a stake in both the continued levels of immunization in this country and the challenge of wiping out the disease worldwide, particularly in developing countries, where measles continues to have a high mortality rate.

Judith Willis is a member of FDA's public affairs staff and editor of the Drug Bulletin.





Whooping Cough Vaccine: Balancing Benefits And Risks



A vaccine for pertussis—or whooping cough—has been under scrutiny in recent months, mainly because its value was questioned in a television documentary. The hour-long TV program originated in the National Broadcasting Co.'s Washington, D.C., outlet. An 11-minute portion of that program was also carried nationwide on NBC's "Today Show."

Pertussis vaccine is given to infants and young children in a series of injections. It's the "P" in what is commonly known as DPT shots. The "D" and the "T" in that series are for diphtheria and tetanus.

To help readers understand both sides of the controversy about the pertussis vaccine, reprinted below is the transcript of a news segment carried by the NBC Washington station as a follow-up of its documentary. Lea Thompson is the TV reporter who made the original documentary. Henry Tennenbaum is an anchorman for the station.

LEA THOMPSON: Reaction continues today to our story on the DPT vaccine. The vaccine is a series of shots almost every child gets before going to school. We have found out that some children have serious reactions to the "P" part of the shot, the part preventing whooping cough. That reaction can be as serious as brain damage.

Many concerned parents have been calling us to say they don't think their children should have to have the shot in order to enroll in school. We've done some checking with local jurisdictions. The law is the same for Maryland, Virginia and the District. All students, before entering kindergarten, must have the vaccine.

The only children that can be exempt are those who get medical waivers from their doctor. These children must have a serious reaction from the "P" part of the shot or a family history of nervous system disorders. Also, children whose parents object to the shot on religious grounds can be exempt. All jurisdictions say exemptions are quite rare.

Since our story, Arlington county school health officials have been in contact with state authorities asking for the DPT vaccine requirement to be reviewed. But the Maryland State Health Department told us today they have had reports of serious reactions to the shot, and that these children are not injected with the "P" part of the vaccine in later shots. The department, however, will continue to require the use of shots.

Maryland Congressman Mike Barnes said today he believes the law in Maryland should be changed to allow parents to choose whether their children should be given the "P" part of the shot.

CONG. MIKE BARNES: Make sure that the legislators and the governor, and everybody else in the state are aware of the problem, and press for action. And, as I have been on other issues, I'm certainly ready and willing to work with people on that.

THOMPSON: Congressman Dan Mica, of Florida.

CONG. DAN MICA: The Congress and FDA, I understand—and we're checking further on exactly how they do this—can issue a statement to the states, to various health authorities: one, about warning; two, about whether or not the federal government encourages it to be mandatory or not. Right now, I would hope that it would not be mandatory in any state until there are some answers.

THOMPSON: Mica offered a resolution to Congress today, calling for hearings on the safety and appropriateness of the DPT vaccine.

Our guest tonight is Dr. Arthur Hull Hayes Jr., commissioner of the Food and Drug Administration, and he is here to respond to our DPT vaccine [story].

Commissioner, I think most parents can understand the need for a nationwide inoculation program to prevent dread childhood diseases. But how do you explain to parents that a vaccine is being mandated that is known to cause some serious problems, yet parents haven't been told?

COMMISSIONER ARTHUR HULL HAYES JR., M.D.: I think there are two questions here. The first one is the mandating of a vaccine. And that is not something in the province of the Food and Drug Administration but, as we have heard, is in the province of the states and the local authorities. What the Public Health Service and the Food and Drug Administration have said, and continue to say, is that we believe all children, unless there is a good medical reason otherwise, should be vaccinated against pertussis.

Whooping cough is a horrible disease, and I'm afraid that in this country we have forgotten what occurred 30 or 40 years ago, before we had an effective vaccine, when six or seven thousand children a year died from the disease, and many more from respiratory problems, pneumonia, encephalitis and brain damage.

THOMPSON: How do you explain the fact that in two countries, Sweden and West Germany, that have quit using the vaccine, there's been no epidemic of the disease and, indeed, the death rate is also way down? How can you compare that?

Now, I understand that in England there have been more cases of whooping cough when they quit using the vaccine but, indeed, the death rate is at an all-time low. Is it possible whooping cough has changed? The disease has changed?

DR. HAYES: We don't have any evidence that whooping cough, as a disease, has changed. There is no question that, as compared to 30 or 40 years ago, there are more things we can do about the disease. There is no cure for it because the disease attacks by a toxin, and there's nothing we can do about that. There are antibiotics today that can shorten the disease. But whether the disease itself has changed, we don't know.

I should point out that populations in different countries, and the vaccines that they use, and the kinds of programs that they have are really quite different, and therefore it is very difficult to compare what has happened in one country or another.

As you mentioned, in England, when they reduced but did not stop the use of vaccine—some 30 or 40 percent of children in England are still vaccinated—for two years they had an epidemic, and then the rate fell. And in fact, what had really happened is that by having thousands of children suffer the ravages of the disease, they then were protected against it any further.

And I suggest that maybe vaccination is a safer and better way of protecting the population against what is a terrible disease than it is to have many of them suffer the disease itself.

THOMPSON: But part of the problem, it seems to me, in the United States is that we have never really done an adequate study to get to the bottom of the fact about how serious whooping cough is, and to get to the bottom of the fact of how many children are having serious reactions from the shot. Is the FDA going to do anything about that?

DR. HAYES: Well, in fact, there not only have been many studies about the importance and severity of the disease, and of the present vaccination, but also many studies about new vaccines made from purified products that we all hope will be less reactive.

Committees—both of the American Academy of Pediatrics, as well as the [Public Health Service] committee that is responsible and [which] meets every year to review data for immunization practices—[are] well aware of the data that are there and encourage the studies that, in fact, continue to go on. There really are no new data.

What we now know about pertussis vaccine has been known for some time. What is important, I think, is to appreciate that one must compare what happens with the vaccination to what would happen, and in fact did happen, and in some countries continues to happen, without the vaccination. And unless one has seen a child who has become very sick or died of whooping cough, it is very easy to forget what a horrible disease it is.

HENRY TENNENBAUM: Dr. Hayes, I don't think anybody is questioning the severity or potential severity of whooping cough. However, I got a call from a friend who says that his daughter, who had recently gotten a pertussis vaccine injection, suffered a reaction. She had no warning whatsoever from the doctor, prior to it, that there might be such a serious reaction. And afterwards, the doctor was prepared to give her another injection. She happened to have had a cold at that time and didn't get the second one.

Why is it that overseas parents are at least warned about the potential severity of this vaccine, and here there's no such requirement?

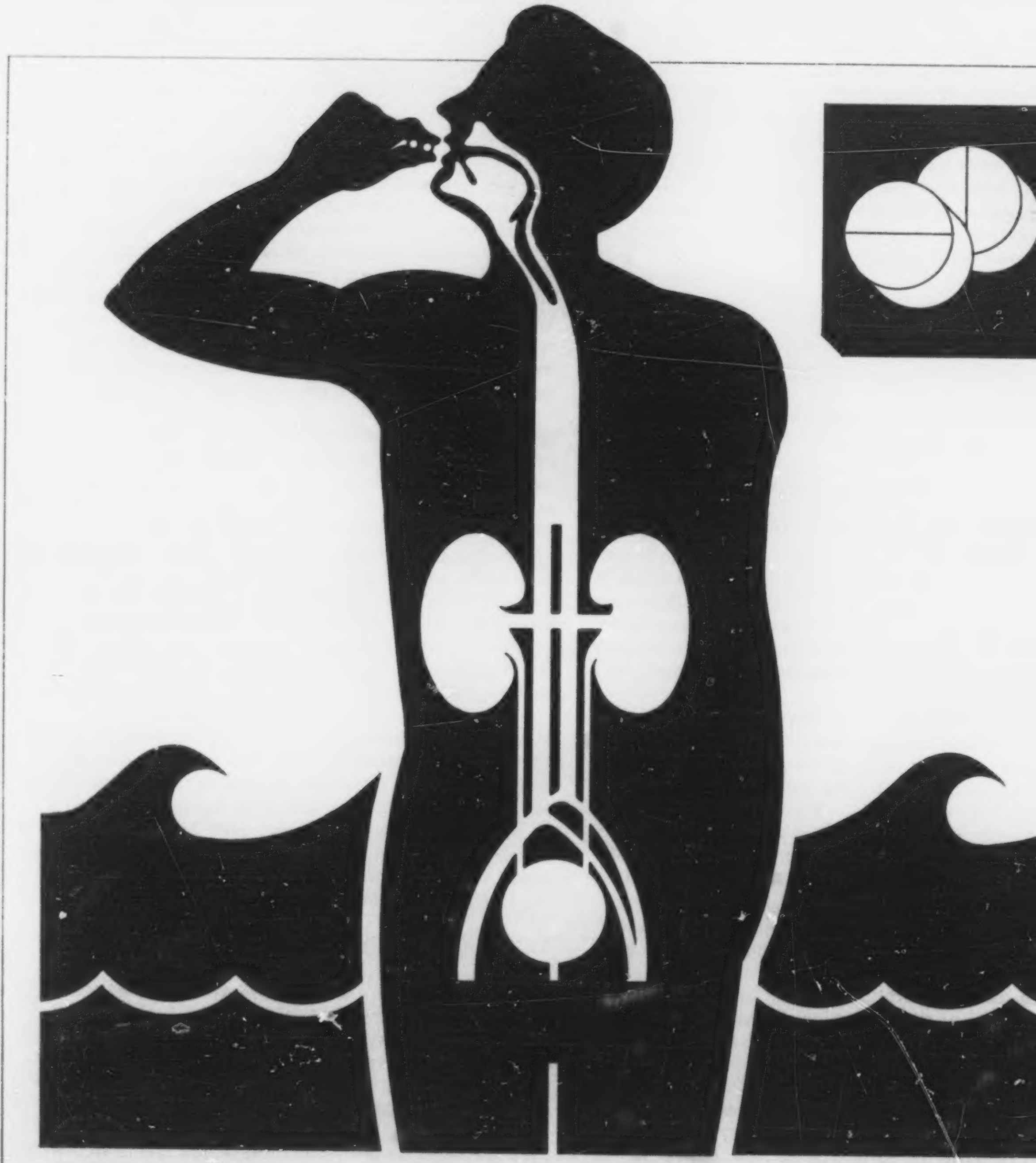
DR. HAYES: There is no question that informing parents about the risks and the benefits of a vaccination or any therapy is terribly important. Indeed, in this country, if one receives the vaccine from federal money—that is, federal money is used to buy the vaccine—there is a special consent and explanatory form, in fact, that is used by many of the states. There's no question that physicians should inform the parents of the children about the risks and benefits . . .

TENNENBAUM: Should that be a requirement?

DR. HAYES: Well, I don't know how one would require exactly what a physician should say. The Academy of Pediatrics in this country has said continuously and stressed to all their members—and the pediatricians are the ones that most frequently give or order such vaccinations—that it is important to discuss it with their patients.

THOMPSON: Commissioner, thank you very much. We're glad that you joined us this evening. Dr. Arthur Hull Hayes Jr., commissioner of the Food and Drug Administration.

DIURETICS



The Importance Of Making Water

by Annabel Hecht

Some people who take diuretics call them "water pills," and it's easy to understand why. The main function of diuretics is to increase the flow of urine, ridding the body of excess water. Diuretics are used to reduce edema (swelling) often caused by conditions such as congestive heart failure, cirrhosis of the liver or premenstrual tension. They also are used to treat hypertension, glaucoma and a type of diabetes known as diabetes insipidus. Sometimes diuretics are given to people who want to lose weight, but the most they can do is help the dieter shed the few pounds that result from excess body fluids.

There are several types of diuretics but all do their work within the kidneys. There they act, not directly on the water, but by increasing elimination of sodium.

Although high sodium intake has been associated with high blood pressure problems, in small amounts sodium is essential to the body and to life. One of its jobs is helping maintain the balance of the body's fluids. The principal organs where this balancing act takes place are the kidneys.

These twin organs are intricate structures, as was explained in "The Kidneys: Complex Cleansing Units," *FDA Consumer*, December 1981-January 1982. Briefly, they are the body's waste removers. Here blood is filtered, unwanted materials are removed, and vital products such as sodium and water are returned as needed to the bloodstream. The return trip takes place through a process called reabsorption, carried out in the millions of tiny nephrons that make up the functioning part of the kidneys.

Normally, the kidneys can maintain the body's fluid balance despite wide variations in salt and water intake. Sometimes, however, the kidneys lose their balancing ability and the sodium and water taken in is not offset by the elimination of an equivalent amount of sodium and water. In other words, sodium intake exceeds sodium output and water is therefore retained in the tissues, creating a definite health problem.

For instance, in the case of congestive heart failure, the heart cannot pump blood effectively and less blood flows to the kidneys. With the lowered blood flow, the kidneys excrete sodium less effectively. In addition, reduced blood flow activates the secretion of aldosterone. All of this means that more sodium and water are reabsorbed, leading to edema.

Diuretics reduce edema by increasing the excretion of sodium and water to achieve a more normal balance. Diuretics do this by blocking sodium reabsorption, thus increasing the sodium excreted. Because water follows the sodium, it too is eliminated in greater amounts.

The most commonly used diuretics can be grouped according to the area of the kidney nephrons where they do their primary work (see figure 1). Some drugs may affect sodium reabsorption in several areas.

The drugs acetazolamide and methazolamide, both sulfonamide derivatives, act at site 1, in the proximal tubule. They block the action of carbonic anhydrase, an enzyme that releases hydrogen from carbon dioxide in the cells of the tubule walls. Hydrogen is exchanged for sodium, allowing the sodium to get back to the bloodstream. Blocking the enzyme prevents formation of hydrogen; hence there is no exchange or reabsorption of sodium. These drugs also decrease the secretion of aqueous humor, the fluid inside the eye. The result is a drop in intraocular pressure. These two drugs are primarily for the treatment of glaucoma and some types of epilepsy. They may also be used to change the acidity of the urine for specific reasons. They are seldom used as diuretics today.

Diuretics that act in the Loop of Henle are called, not surprisingly, loop diuretics. Two loop diuretics currently in use are furosemide and ethacrynic acid. Chemically unrelated, both do the same job—they block the active transport of chloride in the ascending leg of the loop at site 2. This interferes with the passive absorption of sodium. Both also act in the proximal and distal tubules.

Loop diuretics are highly effective drugs usually used when the patient is not being helped by other diuretics or when a rapid removal of water from the body is needed. Furosemide may be used in the treatment of hypertension alone or in combination with another diuretic.

Acting at the third site, in the distal part of the nephron, are the thiazides and related drugs, all of which do their job by promoting the excretion of sodium and chloride in equal amounts. In addition to their diuretic action, the thiazides also have an anti-hypertensive effect and thus are widely used in the treatment of high blood pressure, as well as in the treatment of edema.

These three types of diuretics share a common problem. All cause increased excretion of potassium. This loss can be corrected by eating potassium-rich foods, by taking potassium supplements, or by adding a so-called potassium-sparing diuretic, spironolactone or triamterene, to the dosage regimen.

Spironolactone blocks the hormone aldosterone, thus preventing potassium excretion. Triamterene interferes with the sodium/potassium relationship without involving aldosterone. The amount of potassium spared will depend on how much sodium has reached that site. The potassium-sparing agents are not very effective diuretics when used alone. They are usually used along with thiazide or loop diuretics in the treatment of edema.

Because each type of diuretic behaves in a slightly different way, the decision of which drug to prescribe will depend on the patient's condition and individual needs. The doctor will want to know whether the patient is allergic to sulfa drugs (some diuretics are sulfa derivatives), or if the patient is taking other medications such as corticosteroids, diabetes medicine, digitalis or lithium. Diuretics can interact with such drugs and cause adverse reactions, including an increase in one drug's toxicity or a decrease in another's effectiveness. For instance, the loss of potassium will be increased if a thiazide and a corticosteroid are taken together.

By their nature, diuretics upset the balance of electrolytes: i.e., sodium, chloride, potassium, calcium, magnesium. Therefore, the doctor may call for periodic lab tests to measure these elements in the blood and urine. If necessary, adjustment in treatment can be made to correct imbalances.

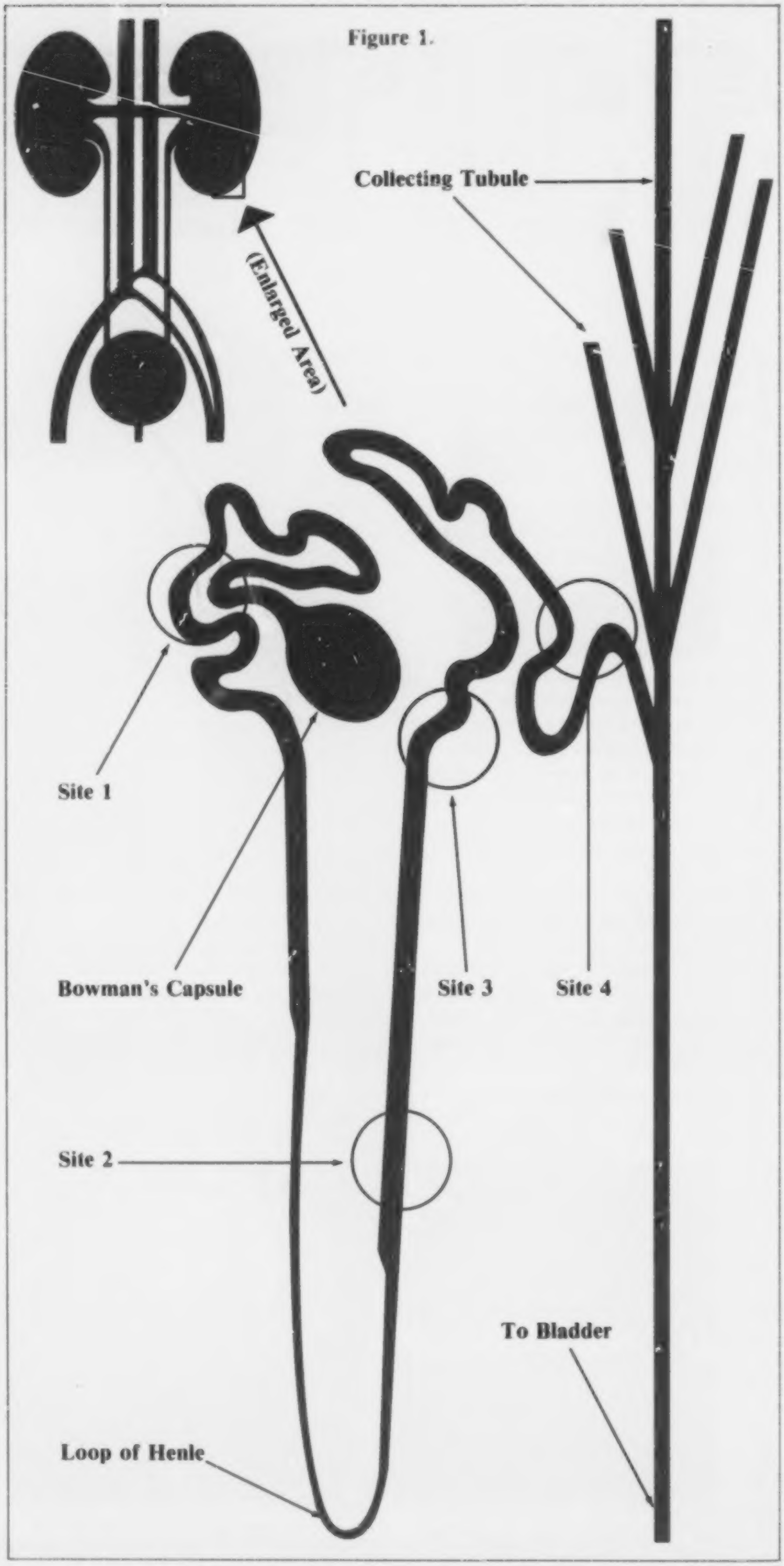
There are other side effects that patients taking diuretics may experience. Drugs that are sulfa derivatives may cause reactions common to all drugs of this type: fever, rash, stomach pain. Acetazolamide may cause a tingling in the extremities or a transient myopia (nearsightedness). Ethacrynic acid may cause deafness, ringing in the ears, vertigo and a sense of fullness in the ear. Furosemide and the thiazides may precipitate gout since they tend to decrease the excretion of uric acid. Potassium loss may be signaled by a dryness of the mouth, increased thirst, unusual tiredness or weakness.

Thiazides and loop diuretics may make the patient lightheaded when he or she rises from a lying or sitting position. Thiazides and triamterene also may increase the sensitivity of the skin to the ultraviolet rays of the sun. Patients on these drugs should take special care to protect themselves when they go out into bright sunlight.

Many of the side effects associated with diuretics go away during treatment as the body adjusts to the drug. Still, patients should consult with their doctor if they experience these or any unexpected or unusual reactions.

Annabel Hecht is a member of FDA's public affairs staff.

Figure 1.



The Sodium-Water Connection

Sodium is reabsorbed at four points and by different mechanisms along the nephron route (see figure 1). The first reabsorption point (site 1) is in the "proximal tubule," just outside the cup-like bulb called Bowman's capsule. Bowman's capsule contains the capillary bed glomerulus where incoming blood is first filtered. The second reabsorption site (site 2) is in the ascending limb of the hairpin-curved Loop of Henle. Sodium also is reabsorbed in two areas (sites 3 and 4) of the "distal tubule," that portion of the nephron closest to the collecting duct. Urine flows through the collecting ducts to the pelvis of the kidney and then is carried from the kidney to the bladder by the ureter.

Sodium is moved through the walls of the kidney tubules by specific pumps in the cells lining the tubules. This process is called active transport. Water, on the other hand, simply follows after the sodium in those areas where the walls of the nephron are permeable, that is, where the water can pass through. In the Loop of Henle, chloride is actively reabsorbed and sodium follows.

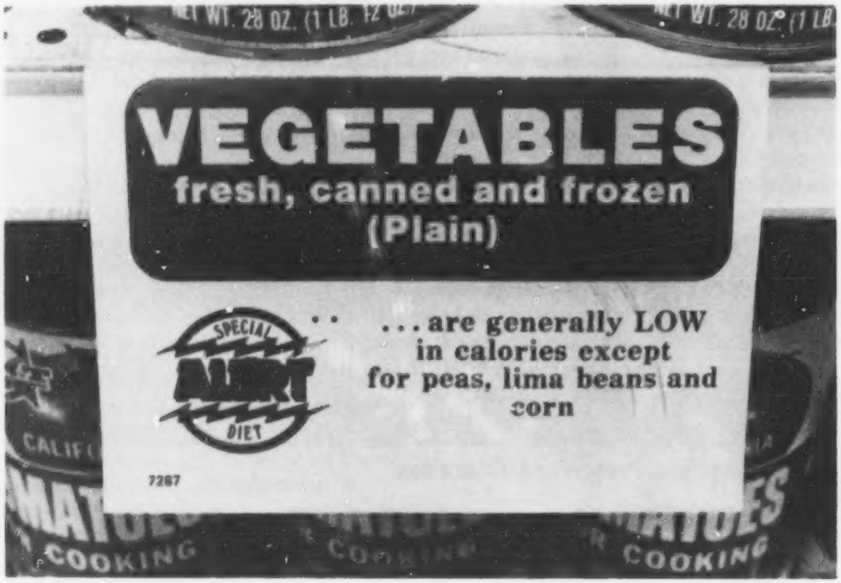
Two hormones play a role in the sodium-water reabsorption process. Both act in the distal portion of the kidney tubules. The first is the anti-diuretic hormone (ADH) secreted by the pituitary gland. The normal action of ADH is to stimulate reabsorption of water from the distal renal tubule and collecting duct. When there is an increase in the level of sodium in the blood, ADH is released from the pituitary gland and promotes water reabsorption by the kidneys to keep sodium diluted to its proper level. A reduction in the concentration of sodium in blood inhibits the pituitary release of ADH, allowing water to go on its way toward elimination.

The second hormone is aldosterone, secreted by the adrenal gland on top of the kidney. Its job is to regulate the reabsorption of sodium and the excretion of potassium at site 4. (Potassium is another electrolyte that is vital to body functions, including muscle contraction.) High levels of aldosterone increase the amount of sodium reabsorbed and the amount of potassium lost. Blocking the hormone has the opposite effect: More sodium is excreted, while potassium is spared.

Some Commonly Prescribed Diuretics

Brand Name	**Generic Name**
Carbonic anhydrase inhibitors	
Diamox	acetazolamide
Neptazane	methazolamide
Loop diuretics	
Lasix	furosemide
Edecrin	ethacrynic acid
Thiazides	
Naturetin	bendroflumethiazide
Aquatag Exna Hydrex	benzthiazide
Diuril SK-Chlorothiazide	chlorothiazide
Hygroton	chlorthalidone
Anhydron Fluidil	cyclothiazide
Esidrix HydroDIURIL Oretic	hydrochlorothiazide
Thiazides	
Diucardin Saluron	hydroflumethiazide
Aquatensen Enduron	methyclothiazide
Diulo Zaroxolyn	metolazone
Renese	polythiazide
Hydromox	quinethazone
Metahydrin Naqua	trichlormethiazide
Potassium-sparing diuretics	
Aldactazide Aldactone	spironolactone
Dyazide Dyrenium	triamterene
Midamor	amiloride

Using The Store Shelf As A Food Label



by Doug Henderson

Last summer Donna Petruska, a legal secretary at a Washington, D.C., law firm, was told she had high blood pressure. Instead of prescribing pills, her doctor placed Donna on a sodium-restricted diet.

But the diet itself was a bitter pill to swallow. Special diets are not always easy to follow because they involve giving up or cutting down on foods that please the palate. In this, Donna's diet was no exception.

Something else made this particular diet frustrating—she didn't know exactly what foods in the marketplace she could or could not eat because the labels on cans and packages do not provide information about sodium content.

Food and Drug Administration labeling regulations do not require that the amount of sodium in a product be declared on the label, and much of the sodium in foods, therefore, is "hidden." Because of this, it's difficult for dieters like Donna to determine how much sodium they are consuming. Result: "I didn't really know how to reduce sodium intake," says Donna.

Just when she was faced with playing hide-and-seek and other guessing games at the grocery store, Donna found out about a new experimental program called Special Diet Alert. The program was being carried out by the Giant Food Co., a grocery chain with 90 stores in Maryland, Virginia and the District of Columbia. Special Diet Alert is a two-year food labeling test program, started in March 1981 with the cooperation of FDA. Its goal is to develop ways to provide certain nutrition information to consumers through "shelf labeling."

Shelf labeling, in this case, means telling what's in the cans or the other food packages—or, rather, what substances or properties they're low in—by means of labels or placards placed near the products themselves, usually on the store shelves. In the case of a person on a low-sodium diet, shelf labeling points out foods that are known to be low in or reduced in sodium content, although the labels on the cans or packages may not say so. Other types of shelf labeling are also aimed at consumers on other special diets, those that specify foods low in or reduced in cholesterol and fat or foods low in or reduced in caloric content.

For its program, Giant has identified around 300 food items, covering a broad range of foods. The products are not necessarily located in a special section of the store, such as a special diet foods corner, but are located alongside other foods that are not labeled or otherwise designated as being low in sodium, cholesterol and fat, or calories. The food products so identified include some of Giant's own house brands and other brands where the processors supplied the information requested by Giant. The rest of the products on the store shelves—those not identified by shelf labeling—are not necessarily higher in sodium, cholesterol and fat, or caloric content than the ones identified as being low. The shelf labeling simply points out those the grocery chain knows to be low in those substances.

"Consumers on restricted diets frequently tell us they have trouble locating foods appropriate for their needs," says Janet Tenney, Giant's nutritionist. "We hope this program makes their food shopping easier."

The firm's program follows FDA regulations in defining low calorie food. For cholesterol content, the firm describes low cholesterol food as having 20 milligrams or less per serving, while reduced cholesterol foods contain 75 percent less cholesterol than the products they replace. Low-fat means two grams or less fat per serving or 10 percent or less fat on a dry weight basis; reduced fat means 50 percent less than in the replaced product. Low-sodium foods contain 25 milligrams or less per serving; moderately low-sodium foods have 100 milligrams or less; and "reduced" means foods have 75 percent less sodium than the replaced product. FDA will soon propose regulations defining low, moderate and reduced sodium. (For a discussion of low calorie foods, see "That Lite Stuff" in the June 1982 *FDA Consumer*.)

"We also want these shoppers to know there are ordinary foods which may be suitable to them," adds Tenney. To a person on a special diet, finding ordinary foods one can eat is important.

To supplement the shelf label information, Giant printed a 24-page brochure, which lists brands of products low or reduced in cholesterol and fat, calories or sodium. In addition, the brochure lists the serving size of each product and the amount of the low or reduced cholesterol and fat or sodium in the product in milligrams per serving. Example: Birds Eye frozen asparagus, half-cup serving, less than 10 milligrams sodium per serving.

For low or reduced calories, the listing is in calories per serving. The Giant brochure also contains hints for cutting down on cholesterol and fat, calories, and sodium such as, "Use garlic and onion *powder*, not garlic and onion *salt*." The information in the brochure allows Donna to plan her shopping list ahead of time, which makes her grocery shopping easier and her special diet less complicated or intimidating.

Giant has promoted the Special Diet Alert program in local newspapers and on radio and TV stations. The firm also mailed over 6,000 packets of information concerning the program to doctors and dietitians who, the company hopes, will pass the information on to their patients on the special diets involved.

The number of Americans on special diets is quite substantial. According to FDA's 1978 Food Labeling Survey, around 20 percent of the population has health problems, such as high blood pressure, obesity and heart disease, which cause them to decide to go on special diets. In addition, over half the people surveyed indicated they were interested in using food labels to avoid certain substances.

Giant says interest in the test program has exceeded its expectations. Tenney reports that in the first two weeks of the program Giant distributed over 100,000 brochures to interested consumers. "We had to halt advertising for a while so more could be printed," she said.

Are there other reasons for such a response to the Special Diet Alert? Many Americans are more concerned about nutrition than they used to be. At least that's what 77 percent of those responding to a 1978 survey by the firm of Yankelovich, Skelly and White indicated. However, most Americans do not want foods of questionable nutritional worth taken off the market since these foods are sometimes gratifying to eat. Instead, consumers want more information provided to help them make trade-offs so they can maintain good eating habits yet continue to eat some favorite foods. Programs such as the Special Diet Alert might allow these consumers not only to make good nutrition decisions, but to make them more quickly.

Making food buying decisions quickly is not as easy as it used to be. Fifty years ago there were only around 500 products to choose from in the neighborhood grocery store. Now the average retail food store offers more than 12,000 items. Thus, consumers have more food choices today but need more useful information to help them make better selections more quickly. However, that means consumers must take the time to figure out how to use that information. Those with an appetite for information often bite off more than they can chew and, in the hectic environment typical in today's crowded grocery stores, they digest very little.

In addition, many consumers have had a hearty meal of TV advertising before they even get to the store. The Northwestern University Medical School, which monitored TV advertising for one week on four Chicago stations, found that over 70 percent of the TV time devoted to food advertising promoted foods generally high in fat, saturated fat, cholesterol, sugar and salt. Advertising displays in stores also compete for a shopper's attention. As a result, today's shoppers get a lot of information but it's not necessarily the kind that helps them make good nutrition decisions.

Lifestyles have changed, too. Today there are more than 25 million working wives in this country, 14 million of whom have children under 18, according to the Bureau of Labor Statistics. These women (and their husbands) have limited time to grocery shop. In addition, teen-agers are leaving home earlier to set up house themselves and are marrying later. Since these singles must take on all the household responsibilities, as well as work and/or go to school, they too have limited time for grocery shopping.

Furthermore, there are more Americans over 65 than ever before. Older Americans are more likely to have special health problems, such as high blood pressure, that require restricted diets.

But will the Giant project meet the changing needs of consumers? Only time will tell. The real test will be at the end of the two-year experimental period when all of the sales data is turned over to FDA for analysis. The major questions, according to Raymond Newberry of FDA's Division of Regulatory Guidance: "Did it get through to the consumers? Did they understand it?"

To answer Newberry's questions, another question must be asked: "Did the sales of the Special Diet Alert foods increase in the Washington stores?" To help find the answer to the question, Giant has matched up the 10 stores in the Washington and northern Virginia area, where the shelf labeling program is being tested, with 10 stores in the Baltimore area (the control group) where no such program exists.

Other grocery retailers may experiment with similar programs, although in the past FDA regulations prevented such innovation from occurring. However, Commissioner Arthur H. Hayes Jr., M.D., in a February speech to the Food Marketing Institute in Washington, D.C., pledged to "remove whatever barriers exist to comprehensive in-store education programs." FDA has already removed a nutrition labeling regulation that stood in the way.

The offending barrier: A regulation which says that if a nutrition claim is made about the product, such as "low in calories" or "low in cholesterol," a nutrition label giving other information must appear on the product under a specific format. In Giant's case, the information on its shelf labels would be deemed a nutrition claim. Since many of the products Giant sought to include in the program contained no nutrition labels, these products, according to the FDA regulation, could not legitimately have been shelf labeled. Therefore, FDA gave Giant an exemption from the rule.

It's all part of the philosophy of government/industry cooperation or what Commissioner Hayes calls the "subsidiary" approach: "The federal government should not perform a function that a state or local government—or, for that matter, the private sector—can do better."

Doug Henderson is a technical writer in FDA's Bureau of Foods.

Who, Why, When And Whe
Of Food Poiso

(And What To Do About Them)

No one would intentionally put poison in his or her food. But sometimes food becomes toxic because of lack of care in processing or because people fail to take steps to prevent foodborne illness. This happens because people often are not aware of the variety of ways food can become contaminated.

The following chart identifies some of the more common organisms that cause food poisoning, the name of the illness each causes, conditions under which the organism thrives in food, symptoms of illness, and methods of preventing food contamination.

Much of the illness classified under the heading "food poisoning" involves the gastrointestinal tract (with one notable exception: botulism causes neurotoxic symptoms involving the respiratory tract). Gastrointestinal symptoms include nausea, vomiting and diarrhea, and are sometimes known as "gastroenteritis." Although the symptoms are all somewhat similar, the organisms or their byproducts that cause the illness are quite different. Those listed in the chart include bacteria, bacterial toxins, viruses, mycotoxins (from molds) and protozoa (one-celled microscopic parasites).

Similarly, the events that result in food poisoning are also different. For instance, some bacteria—such as the *Shigella*—cause illness when large numbers are eaten in food such as potato salad. Because the bacteria multiply rapidly in certain prepared foods left at room temperature, prompt and proper refrigeration of the susceptible foods is the way to prevent illness.

On the other hand, *Clostridium botulinum* bacteria are perfectly harmless to most people if eaten in foods that have not been preserved because they are in the spore, or inactive, stage that survives when there is oxygen in the environment (some infants, however, can become ill from eating botulinum spores). The spores remain inactive unless they are put into the anaerobic (oxygen-less), low-acid environment that they require for activation and growth—a can of green beans, for example. If spores have not been killed during the canning process by application of heat under high pressure, they will reactivate and resume their life cycle, or reproductive process. During this process, the botulinum toxin is manufactured. It's this substance that makes the food poisonous. Contamination of preserved foods may be prevented by following the recommended established canning or other preservation methods.

Viruses and protozoa have their source in the human intestinal tract and can get into food directly from handling by a person who fails to wash his or her hands after a visit to the bathroom. The more personal handling of a food, the greater the chance of contamination and resulting illness. The solution to the problem is to observe proper sanitary habits during food preparation—that is, wash both the hands and raw ingredients thoroughly.

Illness caused by foodborne poisons and poisonous organisms can vary in intensity. The malady can be so mild that it is barely noticed or is passed off as an upset stomach. Again, a lengthy hospitalization might result and, in some cases, the illnesses can kill. But regardless of intensity, food poisoning is unpleasant. It is also something that can be avoided.

—Information compiled by Carol L. Ballentine and Michael L. Herndon of FDA's public affairs staff.

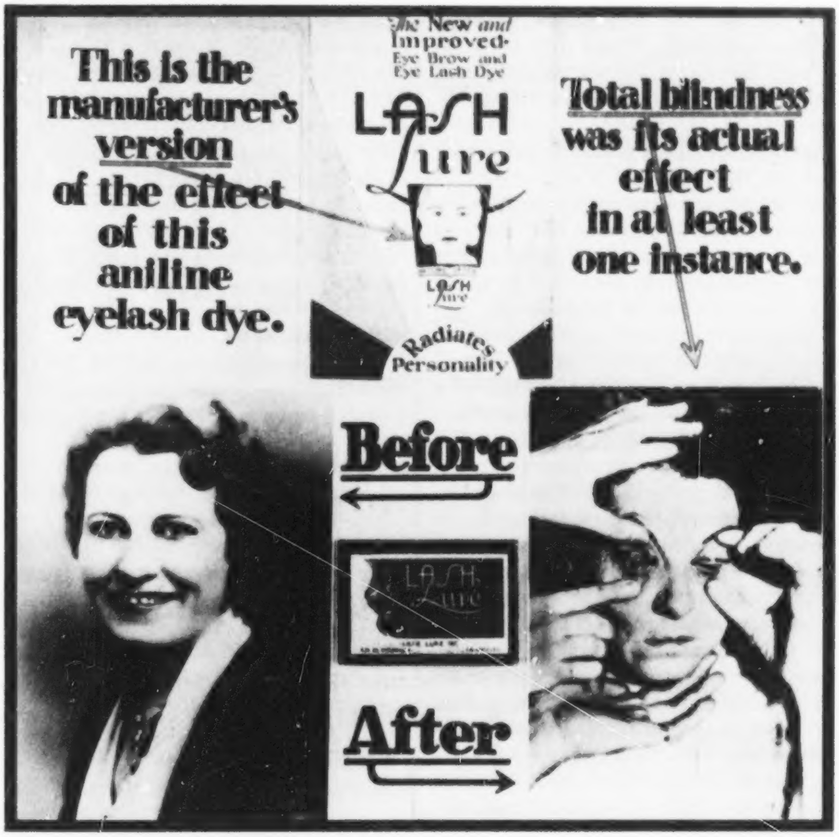
Disease and Organism That Causes It	Source of Illness	Symptoms	Prevention Methods
salmonellosis *Salmonella* (bacteria; more than 1,700 kinds)	May be found in raw meats, poultry, eggs, fish, milk and products made with them. Multiplies rapidly at room temperature.	Onset: 12-48 hours after eating. Nausea, fever, headache, abdominal cramps, diarrhea and sometimes vomiting. Can be fatal in infants, the elderly and the infirm.	**• Handling food in a sanitary manner** **• Thorough cooking of foods** **• Prompt and proper refrigeration of foods**
staphylococcal food poisoning staphylococcal enterotoxin (produced by *Staphylococcus aureus* bacteria)	The toxin is produced when food contaminated with the bacteria is left too long at room temperature. Meats, poultry, egg products; tuna, potato and macaroni salads; and cream-filled pastries are good environments for these bacteria to produce toxin.	Onset: 1-8 hours after eating. Diarrhea, vomiting, nausea, abdominal cramps and prostration. Mimics flu. Lasts 24-48 hours. Rarely fatal.	**• Sanitary food handling practices** **• Prompt and proper refrigeration of foods**
botulism botulinum toxin (produced by *Clostridium botulinum* bacteria)	Bacteria are widespread in the environment. However, bacteria produce toxin only in an anaerobic (oxygen-less) environment of little acidity. Types A, B and F may result from inadequate processing of low-acid canned foods, such as green beans, mushrooms, spinach, olives and beef. Type E normally occurs in fish.	Onset: 8-36 hours after eating. Neurotoxic symptoms, including double vision, inability to swallow, speech difficulty and progressive paralysis of the respiratory system. OBTAIN MEDICAL HELP IMMEDIATELY. BOTULISM CAN BE FATAL.	**• Using proper methods for canning low-acid foods** **• Avoidance of commercially canned low-acid foods with leaky seals or with bent, bulging or broken cans** **• Toxin can be destroyed after a can is opened by boiling contents hard for 10 minutes—NOT RECOMMENDED**

Disease and Organism That Causes It	Source of Illness	Symptoms	Prevention Methods
perfringens food poisoning *Clostridium perfringens* (rod-shaped bacteria)	Bacteria are widespread in environment. Generally found in meat and poultry and dishes made with them. Multiply rapidly when foods are left at room temperature too long. Destroyed by cooking.	Onset: 8-22 hours after eating (usually 12). Abdominal pain and diarrhea. Sometimes nausea and vomiting. Symptoms last a day or less and are usually mild. Can be more serious in older or debilitated people.	• Sanitary handling of foods, especially meat and meat dishes and gravies • Thorough cooking of foods • Prompt and proper refrigeration
shigellosis (bacillary dysentery) *Shigella* (bacteria)	Food becomes contaminated when a human carrier with poor sanitary habits handles liquid or moist food that is then not cooked thoroughly. Organisms multiply in food stored above room temperature. Found in milk and dairy products, poultry, and potato salad.	Onset: 1-7 days after eating. Abdominal pain, cramps, diarrhea, fever, sometimes vomiting, and blood, pus or mucus in stools. Can be serious in infants, the elderly or debilitated people.	• Handling food in a sanitary manner • Proper sewage disposal • Proper refrigeration of foods
campylobacterosis *Campylobacter jejuni* (rod-shaped bacteria)	Bacteria found on poultry, cattle and sheep and can contaminate the meat and milk of these animals. Chief food sources: raw poultry and meat and unpasteurized milk.	Onset: 2-5 days after eating. Diarrhea, abdominal cramping, fever and sometimes bloody stools. Lasts 2-7 days.	• Thorough cooking of foods • Handling food in a sanitary manner • Avoiding unpasteurized milk
gastroenteritis *Yersinia enterocolitica* (non-spore-forming bacteria)	Ubiquitous in nature; carried in food and water. Bacteria multiply rapidly at room temperature, *as well as* at refrigerator temperatures (4° to 9° C). Generally found in raw vegetables, meats, water and unpasteurized milk.	Onset: 2-5 days after eating. Fever, headache, nausea, diarrhea and general malaise. Mimics flu. An important cause of gastroenteritis in children. Can also infect other age groups and, if not treated, can lead to other more serious diseases (such as lymphadenitis, arthritis and Reiter's syndrome).	• Thorough cooking of foods • Sanitizing cutting instruments and cutting boards before preparing foods that are eaten raw • Avoidance of unpasteurized milk and unchlorinated water
cereus food poisoning *Bacillus cereus* (bacteria and possibly their toxin)	Illness may be caused by the bacteria, which are widespread in the environment, or by an enterotoxin created by the bacteria. Found in raw foods. Bacteria multiply rapidly in foods stored at room temperature.	Onset: 1-18 hours after eating. Two types of illness: (1) abdominal pain and diarrhea, and (2) nausea and vomiting. Lasts less than a day.	• Sanitary handling of foods • Thorough cooking of foods • Prompt and adequate refrigeration
cholera *Vibrio cholera* (bacteria)	Found in fish and shellfish harvested from waters contaminated by human sewage. (Bacteria may also occur naturally in Gulf Coast waters.) Chief food sources: seafood, especially types eaten	Onset: 1-3 days. Can range from "subclinical" (a mild uncomplicated bout with diarrhea) to fatal (intense diarrhea with dehydration). Severe cases require hospitalization	• Sanitary handling of foods • Thorough cooking of seafood

Disease and Organism That Causes It	Source of Illness	Symptoms	Prevention Methods
parahaemolyticus food poisoning *Vibrio parahaemolyticus* (bacteria)	Organism lives in salt water and can contaminate fish and shellfish. Thrives in warm weather.	Onset: 15-24 hours after eating. Abdominal pain, nausea, vomiting and diarrhea. Sometimes fever, headache, chills, and mucus and blood in the stools. Lasts 1-2 days. Rarely fatal.	• Sanitary handling of foods • Thorough cooking of seafood
gastrointestinal disease enteroviruses, rotaviruses, parvoviruses	Viruses exist in the intestinal tract of humans and are expelled in feces. Contamination of foods can occur in three ways: (1) when sewage is used to enrich garden/farm soil, (2) by direct hand-to-food contact during the preparation of meals, and (3) when shellfish-growing waters are contaminated by sewage.	Onset: After 24 hours. Severe diarrhea, nausea and vomiting. Respiratory symptoms. Usually lasts 4-5 days but may last for weeks.	• Sanitary handling of foods • Use of pure drinking water • Adequate sewage disposal • Adequate cooking of foods
hepatitis hepatitis A virus	Chief food sources: shellfish harvested from contaminated areas, and foods that are handled a lot during preparation and then eaten raw (such as vegetables).	Jaundice, fatigue. May cause liver damage and death.	• Sanitary handling of foods • Use of pure drinking water • Adequate sewage disposal • Adequate cooking of foods
mycotoxicosis mycotoxins (from molds)	Produced in foods that are relatively high in moisture. Chief food sources: beans and grains that have been stored in a moist place.	May cause liver and/or kidney disease	• Checking foods for visible mold and discarding those that are contaminated • Proper storage of susceptible foods
giardiasis *Giardia lamblia* (flagellated protozoa)	Protozoa exist in the intestinal tract of humans and are expelled in feces. Contamination of foods can occur in two ways: (1) when sewage is used to enrich garden/farm soil, and (2) by direct hand-to-food contact during the preparation of meals. Chief food sources: foods that are handled a lot during preparation.	Diarrhea, abdominal pain, flatulence, abdominal distention, nutritional disturbances, "nervous" symptoms, anorexia, nausea and vomiting.	• Sanitary handling of foods • Avoidance of raw fruits and vegetables in areas where the protozoa is endemic • Proper sewage disposal
amebiasis *Entamoeba histolytica* (amoebic protozoa)		Tenderness over the colon or liver, loose morning stools, recurrent diarrhea, change in bowel habits, "nervous" symptoms, loss of weight and fatigue. Anemia may be present.	• Sanitary handling of foods • Avoidance of raw fruits and vegetables in areas where the protozoa is endemic • Proper sewage disposal

Coal-Tar Dyes Again

by Carol Ballentine


This is the manufacturer's version of the effect of this aniline eyelash dye.
The New and Improved Eye Brow and Eye Lash Dye
LASH Lure
Radiates Personality
Total blindness was its actual effect in at least one instance.
Before
After

Like an outmoded hair style, "Dr. Olbrich's Combinal Dye for Eyebrows/Eyelashes" has aroused memories for many people. For some, the memories are not pleasant.

Dr. Olbrich's Dye is a coal-tar dye for eyebrows and eyelashes. Like the popular coal-tar hair dyes that are similar chemically to the Dr. Olbrich product, the color change is fairly long lasting as compared to temporary colorings such as mascara, eye shadow and eye liner. But although coal-tar hair dyes are legal, coal-tar dyes for eyebrows and eyelashes aren't because they may cause eye injury and even blindness. Most stocks of the Dr. Olbrich product now have been placed under embargo or are being recalled by the U.S. distributors.

The product is uncomfortably reminiscent of Lash Lure, a cosmetic popular in the 1930s that had, in a few cases, a devastating effect. Lash Lure, a synthetic coal-tar dye, was used by many women without ill effect. But for some women the same dye caused an allergic reaction—dermatitis and itching around the eyes. And in 1933 two women suffered worse than that: One 52-year-old woman died after Lash Lure was applied to one eye; she had suffered eight days of violent pain. Another woman—referred to as "Mrs. Brown" in the FDA archives—became blind in both eyes after weeks of intense pain.

Coincidentally, 1933 marked the beginning of the congressional controversy over the need for new—and stronger—food and drug laws. The Lash Lure cases figured prominently in the debate on stronger regulation of cosmetics. At the time, FDA had no legal authority to move against this product because there was no provision in the law prohibiting the sale of cosmetics known to be harmful. Advocates for a stronger law pointed out that knowledge about the deleterious effects of Lash Lure had had only one noticeable effect on the proprietors of beauty salons using the stuff: many instituted a requirement that customers sign an agreement saying they would not sue if they suffered ill effects from the dye.

"Mrs. Brown's" case was used as poignant testimony in the congressional hearings. Pictures of her—before and after Lash Lure—were incorporated into FDA's Chamber of Horrors exhibit, which featured a number of harmful and deceptive products currently on the market. The exhibit was shown to members of the congressional committee conducting the hearings on the proposed food and drug bill.

The woman's story was recounted in detail: One spring day she had Lash Lure applied to her eyelashes at a beauty shop in preparation for a banquet to be held in her honor. Almost immediately her eyes began to sting, and within hours she was suffering pain so intense she had to leave the banquet early. By morning her eyes were swollen shut and draining. Her husband took her to the hospital where she was treated by eight specialists and had several operations, all to no avail. Bedridden for three months, she was hardly able to sleep and eat, and suffered from constant pain that wouldn't yield to analgesics. The pain finally ended but not until the corneas on both eyes had sloughed off, leaving her completely blind.

During the five years of hearings on the food and drug bill, discussion about the use of coal-tar dyes for dyeing the hair and for dyeing eyebrows and eyelashes took place on numerous occasions. One provision proposed for the new law would declare cosmetics to be adulterated (and thus illegal) if they were "injurious to users under customary conditions of use." Many cosmetics manufacturers and associations objected to this provision, which would have effectively outlawed the coal-tar dyes, already known as a cause of allergic reactions in some people such as "Mrs. Brown." One member of the Manufacturers & Distributors of Toilet Preparations argued before the committee that the wording should be made less stringent because the incidence of people with allergic reactions to the dyes was very low. He observed that "one person's bad reaction to a popular product was as uncommon as a person having a bad reaction to oysters." Representative Virgil Chapman from Kentucky, who was chairman of the hearings, replied, "Did you ever hear of oysters putting anybody's eyes out?"

The provision remained in the food and drug bill, and the hair dye lobby took another approach. They argued that if the coal-tar hair dyes were made illegal it would give rise to a bootleg hair-dye industry that would be impossible to control. This argument apparently had some effect. Several revisions later, an exemption was written into the cosmetics section of the bill declaring that coal-tar dyes for hair were not subject to the adulteration provision of the law as long as the products carried a warning on the label about possible allergic reactions, as well as instructions to users for doing a test ("the patch test") to see if they had such a reaction. However, the coal-tar exemption for hair dyes did not apply to dyes for eyelashes and eyebrows. When the law was passed, such dyes became illegal.

The new Food, Drug, and Cosmetic Act was passed in 1938, and Lash Lure was the first product seized under its authority, approximately five years after the injuries were reported.

In the current case of "Dr. Olbrich's Combinal Dye for Eyebrows/Eyelashes," getting the product off the market didn't take anywhere near as long. FDA's New York district received a sample of the dye in November 1981 from a doctor in New York City. The doctor said he suspected the product contained coal-tar dyes, and analysis by the district confirmed it. Investigators traced the origin and found that the distributor, Dynex International Ltd., New York, N.Y., had imported the product from W. Pauli, a company in Vienna, Austria. Dynex then sold the dye to beauty parlors and salons.

At the district's request, New York state authorities embargoed the 3,057 quarter-ounce tubes of the product stored at the Dynex warehouse (enough to dye the lashes of up to 100,000 persons). The matter was not totally resolved, however. About the same time the doctor submitted his sample to FDA the Los Angeles district received a complaint from a woman in Fremont, Calif., who said she had suffered erosion of the left cornea after a beautician applied the dye to her lashes. She suffered no permanent damage to vision, but the incident showed that the product was more widely distributed than FDA had thought. In April the agency issued a warning to the public about the product, stating that it could cause permanent injury to the eyes, including blindness. FDA also issued an import alert to all districts to prevent further importation of the dyes. As of the middle of May, nine U.S. firms, including Dynex, had recalled the product.

Carol Ballentine is a member of FDA's public affairs staff.

> *"A cosmetic is adulterated if it contains a poisonous or deleterious substance which may cause it to be injurious to users under customary conditions of use . . . . However, coal-tar hair dyes which may irritate the skin are not subject to the adulteration or color additives provisions of the law when the product bears the caution statement prescribed under the law and "patch test" instructions are included with the product. This provision does not apply to products intended for dyeing the eyelashes or eyebrows. Such products may not contain any coal-tar color."*
>
> —Federal Food, Drug, and Cosmetic Act

Too Much Variety

Variety may be the spice of life, but it is not appropriate in a bottle of pills. Each tablet should contain essentially the same amount of active ingredient, or else the pill-taker may receive a dose that is too high or too low.

As part of a drug surveillance program, FDA analyzes various drugs to determine whether they contain the quantity of active ingredients stated on the label. As a standard for the amount of variation that is acceptable, FDA refers to the U.S. Pharmacopoeia's content uniformity requirements for individual drugs.

In New Jersey over 90,000 tablets of an anti-hypertensive medication were seized, based on FDA analyses that showed the tablets failed to meet USP standards for uniformity. Involved were two lots of tablets containing a combination of hydralazine hydrochloride, hydrochlorothiazide and reserpine, manufactured by Zenith Laboratories, Northvale, N.J. They were taken into custody by a U.S. marshal for the District Court of New Jersey.

Samples of one lot were originally taken for the drug surveillance program by FDA's **Newark district** office.

An analysis by the agency's National Center for Drug Analysis in St. Louis showed that the ingredient reserpine failed to meet USP content uniformity requirements. The reserpine in 60 tablets tested ranged as low as 59.5 percent and as high as 123 percent of the amount declared on the label. A total of 12 tablets were outside USP's allowable range of 85 percent to 115 percent. A confirmatory analysis by a different FDA chemist showed a range of 69 percent to 107 percent of the declared potency among 30 additional tablets, 15 of those being outside allowable limits.

The district took samples of a second lot and analyses by the Center for Drug Analysis revealed similar results. At FDA's request, the original sampled lot was placed under embargo by the New Jersey State Department of Health, and the company agreed to hold the second lot. After the seizure, the court ordered destruction of the tablets when the company took no action to claim the product.

Problem Pink Peppercorns

Some American gourmet cooks have learned about a new spice imported from France, but until it is proven safe they will have a tough time getting it. No more imports of pink or red peppercorns will be admitted into this country until FDA receives evidence of the product's safety for food use.

Allegedly grown exclusively on a French island off the coast of Madagascar, pink peppercorns are prized by restaurateurs and epicures for their slightly sweet flavor. Imported peppercorns examined by FDA's Bureau of Foods were identified as berries from a plant also found in the United States, particularly in Florida. Skin contact with or inhalation of parts of the plant have been shown to cause allergy-like reactions similar to severe poison ivy plus asthma-like reactions in some individuals.

Pink peppercorns roused official curiosity last November after newspapers reported that persons who ingested the berries had suffered "tightness" in the chest. After reading such news reports, a New York importer asked FDA's **New York district** office whether the product was safe to sell. The district took a sample and sent it to the Bureau of Foods laboratories in Washington, D.C., for analysis. The sample was confirmed to be a plant with the botanical name *Schinus terebinthifolius*. Since this plant is not approved as a food additive and is not generally recognized as safe for use in food, the importer agreed to recall 106 pounds of peppercorns that had already been distributed. Another 224 pounds in stock were placed under embargo by New York state authorities at FDA's request.

Peppercorns

Several other importers have recalled pink peppercorns and related products such as peppercorn oil and mustard. FDA has alerted its field staff to detain (refuse entry to) all shipments of such products until further notice.

In February, the Bureau of Foods convened its Health Hazard Evaluation Board to examine data on the effects of *S. terebinthifolius*. The board determined that products of the plant should be considered a moderate hazard to susceptible individuals, at least until more information is available. Skin or inhalation contact with the plant may cause problems such as rashes, asthma-like attacks, headaches, swollen eyelids, sore throat, upset stomach, diarrhea and hemorrhoids in some people. Although information about the effects in humans of eating parts of the plant is scant, there is evidence linking it to deaths of birds and fish.

The French Embassy in Washington, D.C., has submitted information to FDA to support a claim that although the French plants are related to the American variety, the berries of the French plant are not toxic or harmful. However, the data were insufficient to confirm the safety of the French plant, and FDA has asked for additional information.

Fish: Illegal and Bad

The health department of Ulster County, N.Y., handed FDA a double mystery earlier this year when it asked the agency to assist in an apparent food poisoning incident.

The first: Why did two men become ill shortly after eating a fish dinner at a restaurant in New Paltz, N.Y.?

The answer, an investigator from FDA's **Newburgh (N.Y.) resident post** found, was that the two were suffering from scombroid poisoning. This is a severe gastric illness that results from eating fish that are high in the chemical compound histamine.

Symptoms of such poisoning include chills, fever, muscular weakness, aching joints and paralysis. Sometimes death can result. The toxic histamine is formed by bacterial action in the flesh of the fish. Histamine is found in plant and animal tissue, is a potent gastric stimulant, and in concentrated amounts can cause scombroid poisoning.

After the diagnosis, the Ulster health department embargoed the large lot of fish still remaining at the premises of the dealer who had supplied the restaurant. Fish from the restaurant and the dealer were analyzed for histamine by FDA's **Buffalo district** laboratory. Both showed histamine present, with the sample from the restaurant the highest.

The second question then arose: Why did the fish shown on the menu as red snapper, an ocean delicacy, have high levels of histamine, unusual for this kind of fish?

The answer: It was not red snapper, but mahimahi, a fish taken off the Pacific coast of South America. It is so predictably high in toxic histamine that FDA regulations prohibit its import in the United States.

FDA found that the fish mislabeled red snapper had been shipped from

Ecuador and processed (filleted and packed) in Panama. It had been imported by Pan American Seafoods of Fairfield, N.J. Had the fish been labeled mahimahi, it would never have made it ashore.

Because the fish was imported illegally, FDA requested a recall by the distributor, which was done. The recall was given an FDA Class II designation, meaning that the product was a likely health threat to consumers.

Firm Finds Flaws

Several generations of Southern families have known the Sauer line of sauces, spices and other food items. Apparently, its good reputation means something to the firm, because it runs daily tests on the peanut butter produced at its Mauldin, S.C., plant. Recent tests by Sauer found high levels of aflatoxin in that product, and so the company recalled an entire week's production, some 20,000 pounds valued at more than $16,000.

Aflatoxin is a toxic substance produced by mold (*Aspergillus flavus*) that attacks certain nuts, corn and other field crops when growing and storage conditions are right. Right, that is, for the mold. FDA has set a limit of 20 parts per billion for aflatoxin in peanut butter; Sauer was finding levels of up to 57 parts per billion.

The higher levels showed up in Sauer's laboratory tests after a new shipment of peanuts from Virginia was added to the production line. The nuts had been certified by the U.S. Department of Agriculture as being acceptable in terms of aflatoxin, but the Sauer tests showed otherwise.

Sweet It Wasn't

Hoping to avoid a complete loss on a quantity of flour and sugar that had been contaminated by insects, a Nebraska firm tried to sell the sugar as bee food and as an ingredient in cattle food but found no takers.

The contamination was discovered at the John J. Meier Co., Omaha, in October 1981 during an inspection by FDA's **Kansas City district** office. The company operates a warehouse and is a distributor of mainly flour and sugar sold in bulk sizes to bakeries.

The investigators found beetles in the seams on the outside of some of the bags of flour and sugar. A closer examination revealed the contents of some of the bags were also insect infested. Insects can get into the bags by drilling small holes or squeezing through holes made where the bags are stitched.

The company destroyed all the contaminated flour, which included 25 fifty-pound bags. The sugar totaled 259 one hundred-pound bags, valued at approximately $6,000. The company notified various apiaries and animal food manufacturers in Nebraska that the 259 bags were for sale. But no buyers came forth.

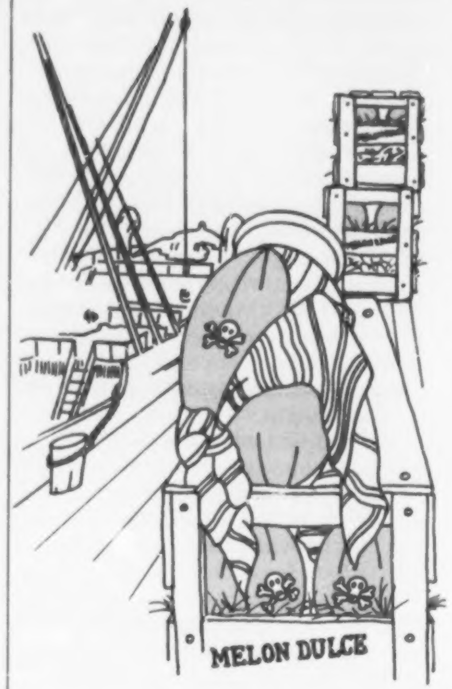
Consequently, the lot was hauled to a city dump. FDA representatives were on hand to witness and verify the burial.

Honeydews/Honey-don'ts

When severe weather conditions in the United States affect the domestic fruit and vegetable crop, foreign produce often fills the void in U.S. supermarket bins. But some foreign produce contains illegal pesticide residues because the producers, who do not ship regularly to the United States, are unfamiliar with requirements enforced by FDA for foods marketed in this country.

This was the case last winter after a severe freeze in Florida and Texas and heavy rainfall in southern California caused widespread destruction of produce crops. Expecting that increased shipments of fresh fruits and vegetables would soon arrive from South America, FDA issued an import alert to all its district offices to gear up their inspection capability.

FDA's **New York Regional Laboratory** in Brooklyn, testing samples of fresh fruits and vegetables entering the Port of New York, found residues of acephate in honeydews from Venezuela. Acephate is used on fruits and vegetables to control insects. It is allowed at certain levels in some fruits and vegetables but forbidden at any level in honeydews. The acephate in the melons totaled 0.43 parts per million, and the shipment was denied entry into the country.



Double Trouble

A fillet is a boneless piece or slice of meat or fish. It is not simply a fish with its head cut off. Nevertheless, over 4,000 pounds of frozen fish of the headless variety found in a warehouse in Columbus, Ga., were mislabeled as "fillets."

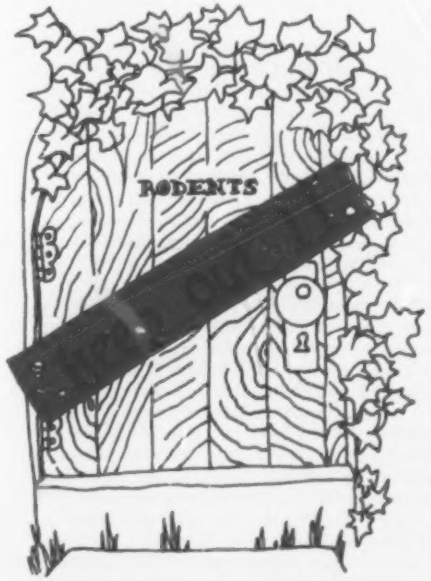
Another, more serious problem existed. The fish showed signs of decomposition. FDA's **Atlanta district** first learned of the situation from a U.S. Department of Agriculture inspector who had visited the warehouse and had seen—or possibly smelled—the fish. The inspector called FDA, who quickly sent an investigator to take samples. Atlanta's regional laboratory confirmed the decomposition through organoleptic (sensory) testing.

FDA's evidence resulted in the seizure by a U.S. marshal of 81 cases of frozen whiting processed by Eastern Point Seafoods Inc. of Gloucester, Mass., and distributed by Southern Foods of Columbus, Ga. Charges included both adulteration and misbranding. The distributor took no action to claim the products, and the frozen whiting was destroyed under court order.

How's That?

Progressive Foods, a bakery in Memphis, Tenn., was told by an FDA inspector in November 1981 that the firm had a problem because rodents were getting into the bakery's warehouse and contaminating cake flour and pie dough mix. Some 3,500 pounds of these raw materials were found contaminated at that time and were destroyed by the company.

A month later the inspector from the **Memphis resident post** came by again and found that the firm had cleaned up the storage area to some extent and had sealed some rodent entrances. But the warehouse sanitation was still short of what it should be. This time 750 pounds of raw materials contaminated since the earlier inspection were destroyed.



Two FDA inspections a month apart should have convinced the firm that improvements were needed. But it took one more FDA-initiated action—seizure of the entire warehouse stock of raw materials (10,000 pounds)—to get the message across.

This time Progressive Foods understood. The company sorted through the seized cake flour and pie dough, found two bags of flour and one of pie mix that were contaminated, and destroyed them. The rest of the stock was acceptable. The company also made the final needed improvements in its warehouse operation to bring it up to standards.

DMSO

The chemical compound dimethyl sulfoxide (DMSO) needs little introduction. It is a liquid residue of wood pulp processing that has an unproven reputation as a wonder drug, usually as an applied treatment for arthritis. But it has only one accepted medical use for humans: in dilute form and by prescription, to treat a rare kind of bladder condition. It is also a veterinary drug.

The historic use for DMSO has been as an industrial solvent and degreaser, which it does well since it is a potent chemical.

This was pretty much the situation with DMSO until 15 or 20 years ago, when it was pushed onto the national scene by adroit and deceptive maneuvering and testimonial advertising.

Some of that more recent activity can be traced to a little retail outlet on the Puyallup Reservation near Tacoma, Wash. The outlet, known as the Smoke Shop and operated by B. J. Enterprises, came to FDA's attention two years ago by offering "degreaser solvent DMSO" to retail customers. The promotion began as a local effort, and soon spread across the Pacific Northwest, with other sellers dispensing the drug from storefronts, the backs of trucks, and wherever customers could be found.

Sensing profits, some entrepreneurs formed Nordic Laboratories/Solvent Sales to organize this activity. They placed newspaper ads throughout the country, tied into tape-recorded, toll-free telephone messages that gave the medical virtues of the degreaser and the post office box where orders could be sent.

In 1981, FDA's Seattle district office recommended seizure of DMSO stocks held by Solvent Sales and by the Smoke Shop, for making medical claims for an industrial product.

It took some months for FDA to accumulate evidence. Investigators made many DMSO purchases to establish the ties between the distributor, the retail outlet, the taped medical claims and the post office boxes. They assembled a file of affidavits and other documentation, showing that the DMSO was an impure, industrial grade chemical being sold without prescription for medical purposes. With the case well supported, FDA moved against the Solvent Sales operation with court orders and U.S. marshals.

Solvent Sales management was uncooperative at first, denying that it had any DMSO except what was in the office. Then company officials remembered that there was some at an adjoining warehouse, which the marshals seized. Then they led FDA to a contract firm who did work for them, where marshals found and seized 30,000 bottles waiting to be filled. Then someone did some more remembering, because four full drums of DMSO and two empties appeared unannounced on the sidewalk outside the Solvent Sales office. These also were seized. Total seizures at Solvent Sales locations, valued at more than $200,000, took FDA and the marshals over a week.

Much the same sequence went on at B. J. Enterprises (the Smoke Shop). The owners of the shop, where 38 bottles were seized, said they knew nothing about a second location for bottling and storing DMSO. But FDA and the marshals did, and at that location they found drums and bottles of it, valued at $80,000.

What the agency also found at the second bottling plant made the effort even more important.

The B. J. Enterprise people were sharing the facility with a firm that packed industrial chemicals, and the mixing and filling equipment and drums were being used interchangeably for DMSO and corrosive chemicals. If the DMSO was impure before, after going through this contaminated equipment, it could have become downright dangerous.

—This small sample of reports from the field was compiled and written by Marti Asner, Louise Fenner and Richard Thompson.

Seizures and Postal Service Cases

FILED SEIZURE ACTIONS charge violations of the Federal Food, Drug, and Cosmetic Act and are initiated based upon FDA recommendations. A seizure action is commenced by the filing in the U.S. district court where the goods are located. A U.S. marshal is then directed by the court to take possession of the goods, removing the product from commerce, until the matter is resolved.

A total of 10 actions to remove from the consumer market products charged to be violative was reported in April. These actions included 9 seizures of foods: 5 involved charges concerning contamination and insanitary handling, and 4 involved charges concerning economic and labeling violations. Others included 1 of drugs.

PRODUCT, DISTRICT & DATE FILED	FIRM & PLACE OF BUSINESS	CHARGES
	FOOD/Contamination, Spoilage, Insanitary Handling	
Candy bars, gums, candy cups, cookies, candy wafers and other confectionary stocks/U.S. District Court for the Western District of New York 4/1/82	Shosho Brothers Inc./Buffalo, N.Y.	Products have been held under insanitary conditions, and some candy cups and caramels contain rodent filth.
Cocoa powder/U.S. District Court for the District of Puerto Rico 4/6/82	Shipped from Baltimore, Md.	Product contains insects.
Mole/U.S. District Court for the Northern District of Illinois 3/30/82	Dona Maria S.A./San Luis Potosi, Mexico	Product contains insect and rodent filth. Required label information is not in terms likely to be read and understood, since the labeling is not in English.
Mole/U.S. District Court for the Northern District of Illinois 3/30/82	Dona Maria S.A./San Luis Potosi, Mexico	Product contains insect filth. Required label information is not in terms likely to be read and understood, since the label is not in English.
Peanuts, shelled/U.S. District Court for the Northern District of California 3/15/82	Art's Trading Co./San Francisco, Calif.	Product contains rodent filth and has also been held under insanitary conditions.
	FOOD/Economic and Labeling Violations	
Frozen concentrated orange juice (FCOJ)/U.S. District Court for the Southern District of Iowa 2/4/82	Fresh Pak Foods/Weslaco, Texas	Product contains turmeric. Labeling is false and misleading, fails to conform to standard of identity, and also fails to state product contains turmeric. The color turmeric had been added to the product to make it appear better or of greater value; the product contains the non-conforming color additive turmeric; the labeling was false and misleading as to the identity of the article; the article fails to conform to the definition and standard of identity for frozen concentrated orange juice; and the article contains the artificial coloring turmeric and its label fails to state that fact.
Concentrated orange juice for manufacturing/U.S. District Court for the Northern District of California 2/24/82	Fresh Pak Foods Inc./McAllen, Texas	The color turmeric has been added so as to make the product appear better or of greater value than the product is; the product contains the non-conforming color additive turmeric, since there is no regulation permitting turmeric in the product; the product's labeling is false and misleading as to the product's identity; the product fails to conform to the definition and standard of identity for concentrated orange juice for manufacturing; and the product contains the artificial color turmeric and the label fails to state that fact.
"Honey"/U.S. District Court for the District of Nevada 3/5/82	J. H. Pilgrim/Dekalb, Miss.	Glucose and/or corn syrup has been substituted for honey; labels are false and misleading as to identity of product; some lots lacked required label statements; and the labels of some lots were in violation of the Fair Packaging and Labeling Act.
"Maple" syrup, Pure Pioneer/U.S. District Court for the District of Nevada 3/8/82	Dewey Clark/Philadelphia, Miss.	Corn syrup has been substituted for maple syrup; labeling is false and misleading since it is not maple syrup; failure to conform to definition and standard of identity for maple syrup since product is made with a syrup other than that from the maple tree.

PRODUCT, DISTRICT & DATE FILED	FIRM & PLACE OF BUSINESS	CHARGES
	DRUGS/Human	
Meclizine hydrochloride tablets/U.S. District Court for the Western District of Kentucky 3/19/82	Camall Co./Washington, Mich.	Product is subpotent. Circumstances used for product's manufacture and processing failed to conform with current good manufacturing practice

U.S. POSTAL SERVICE

actions taken in medical cases as authorized in the Mail Fraud Statute (18 U.S.C. 1341) and/or the False Representation Statute (39 U.S.C. 3005) as reported by the Chief Postal Inspector.

Complaints Filed by Law Department Under 39 U.S.C. (False Representation)

November 10, 1981: **Bio-Thene/100,** Station Plaza East, Great Neck, N.Y. Advertising and sale through the mail of the product "Bio-Thene." The ad states, in part, "burns away more body fat each day than 15 hours of non-stop exercise! Shrinks down your waistline as much as a full size smaller in just 24 hours . . . 4 sizes smaller in just 14 days."

November 10, 1981: **Nature's Harvest Inc.,** 95 M South Hoffman Lane, Central Islip, N.Y. Advertising and sale through the mail of the product "Super Oxide Dismutase." The ad states, in part, "anti-aging basics in a bottle . . . taking SOD tablets just might be the easiest way available to fight back at the debilitating effects of free radicals."

November 10, 1981: **Specialty Diet Sales Inc.,** 1919 Broadhollow Road, Farmingdale, N.Y. Advertising and sale through the mail of the product "Fat-Melting Factor," representing the ability to "peel off a pound a day without missing a single meal! You must see dramatic results in just 24 hours . . . lose up to 6 lbs the first 48 hours . . . works faster, easier than if you ran 10 miles a day . . . or did 300 sit-ups each morning."

November 12, 1981: **The Mail Order Discount Shopper,** 400 Commonwealth Avenue, Boston, Mass. Advertising and sale through the mail of the product "Control Tablets," representing the ability to "help you retain less fluids . . . contain an ingredient that has been reported to help burn up fat faster."

November 12, 1981: **Eyes of the Century,** 540 California Street, Stockton, Calif. Advertising and sale through the mail of the product "Eye Weights." The ad states, in part, "eyesight improved quickly; wrinkles disappear; circulation around the eyes dramatically increased; and you can become healthier and happier."

November 13, 1981: **Health Product Services Inc.,** 3430 E. Tropicana, Las Vegas, Nev. Advertising and sale through the mail of the product "XPL-170," representing the ability to "lose 20 to 60 pounds or more in the next 3 weeks or you pay nothing."

November 13, 1981: **Nutrition Headquarters,** 104 West Jackson Street, Carbondale, Ill. Advertising and sale through the mail of the product "Manotex Tablets." The ad states, in part, "a scientific formula of pure food substances for relieving the symptoms of benign prostatis hypertrophy."

November 13, 1981: **London Diet Research Ltd.,** Station Plaza East, Great Neck, N.Y. Advertising and sale through the mail of the product "Mira/Slim 100," representing the ability to "lose up to 4 sizes in just 14 days on this program . . . losses of as much as 1 pound gone every 8 hours."

December 8, 1981: **Richelieu Pharmacals,** 4 Richelieu Plaza, Canton, Ohio. Advertising and sale through the mail of the product "Natural Slim Pill Plan," representing the ability to "control hunger and speed fat burn-off naturally . . . lose up to 6 pounds in 48 hours . . . 13 pounds in 7 days."

December 10, 1981: **Weight Loss Center,** 2 Richelieu Plaza, Canton, Ohio. Advertising and sale through the mail of the product "The Quick Loss Fat Burn System." The ad states, in part, "medical science discovery that speeds up your fat burning metabolism. Your body is gently converted into a high speed fat burning system . . . no strenuous exercise, no weird fad dieting."

December 14, 1981: **Ace's Distributing Co.,** 1935 Newberry Street, Williamsport, Pa. Advertising and sale through the mail of "Stimulants." These stimulants are being sold as look-alike narcotics.

December 14, 1981: **Klein's Distributing,** 525 Summit Drive, Lewistown, Pa. Advertising and sale through the mail of "Stimulants." These stimulants are being sold as look-alike narcotics.

December 28, 1981: **United Research Products,** 249 S. Highway 101, Solana Beach, Calif. Advertising and sale through the mail of the product "Isa Thermetrics Reducing Belt," representing the ability to "help rid you of unwanted inches faster than ever before . . . helps promote water loss around your waist and stomach."

December 28, 1981: **United Research Products,** P. O. Box 2344, Leucadia, Calif. Advertising and sale through the mail of the product "Reducing Shorts." The ad states, in part, "sauna short's gentle contact with your skin promotes water loss to help shrink your entire midsection, hips, thighs, and buttocks . . . most natural ways to trim and firm the body."

False Representation Orders Issued by Judicial Officer Under 39 U.S.C. 3005

December 14, 1981: Against **Jules J. Garfield,** 1626 N. Wilcox, Suite 366, Hollywood, Calif. Satisfactory evidence was presented to the Postal Service that Jules J. Garfield and its representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Placenta Big Bosom Creme with Magnum Cup Expander." The ad states, in part, "The A, B, C (and D's) of Breast Enlargement . . . increase your bust up to 6 inches and 3 cup sizes."

December 14, 1981: Against **Rockwell Scientific Industries,** 210 Fifth Avenue, New York, N.Y. Satisfactory evidence was presented to the Postal Service that Rockwell Scientific Industries and its representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Astro Triplex," representing the ability to "enlarge your bosom 3 full cup sizes in only 1 week!!!"

December 22, 1981: Against **Eyes of the Century,** 540 California Street, Stockton, Calif. Satisfactory evidence was presented to the Postal Service that Eyes of the Century and its agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Eye Weights." The ad states, in part, "our research has found that many vision problems can be a direct result of weak, soggy, baggy tissue around the eye. Benefits from regular use of the product: eyesight improved quickly; wrinkles disappear; circulation around the eyes dramatically increased; and you can become healthier and happier."

December 23, 1981: Against **Ritz (MVCO Inc.),** P.O. Box 1641, Bridgeview, Ill. Satisfactory evidence was presented to the Postal Service that Ritz and its representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Black Beauty Diet Aid Capsules," representing the ability to lose weight. "Now you can have the figure . . . and the life you really deserve! We can make it happen for you. Lose excess pounds and inches without heavy dieting or strenuous exercising. Black Beauty one a day capsules will help you to lose as many pounds as you need."

December 30, 1981: Against **Net,** Box 13422, Tucson, Ariz. Satisfactory evidence was presented to the Postal Service that Net and its agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Breast Enlargement Program," representing "a revolutionary technique to 'naturally' enlarge your breast up to a full cup size . . . you can quickly and easily achieve wonderous breast development results with this simple new proven method."

Notices of Judgment

NOTICES OF JUDGMENT on Seizure Actions

FOOD/Poisonous and Deleterious Substance

Rye grain, in three railcars, at Minneapolis, Dist. Minn.

Charged 1-6-81: when shipped by Mott Equity Exchange, Mott, N.D., the article contained the pesticide chemical malathion in excess of the prescribed tolerance for such pesticide chemical on rye; 402(a)(2)(B). A default decree ordered the article destroyed. Subsequently, the decree was amended to allow salvaging of the article. (F.D.C. No. 63288; S. No. 81-218-496; N.J. No. 1)

FOOD/Contamination, Spoilage, Insanitary Handling

Cherry pulp concentrate, frozen, at Clermont, N. Dist. N.Y.

Charged 10-22-81: while held by Clermont Fruit Packers Inc., Clermont, N.Y., who had produced the article using interstate cherries, the article contained rotten cherries; 402(a)(3). Default decree ordered destruction. (F.D.C. No. 63568; S. No. 81-256-575; N.J. No. 2)

Lemon peel, dried, at Seattle, W. Dist. Wash.

Charged 4-6-81: while held by Western Herb Farms Inc., Seattle, Wash., the article contained insect and rodent filth—402(a)(3); and the article had been held under insanitary conditions—402(a)(4). Default decree ordered destruction. (F.D.C. No. 63428; S. No. 81-177-031; N.J. No. 3)

Pinto beans, at Oklahoma City, W. Dist. Okla.

Charged 3-11-81: while held by Tanaka Produce Inc., Oklahoma City, Okla., the article contained rodent urine and had been held under insanitary conditions; 402(a)(3), 402(a)(4). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63394; S. No. 81-211-594; N.J. No. 4)

Raisins, Pyramid Brand, at New York, S. Dist. N.Y.

Charged 3-31-82: when shipped by Pyramid Packing Inc., Selma, Calif., the article contained insect filth; 402(a)(3). Default decree ordered destruction. (F.D.C. No. 63603; S. No. 82-128-269; N.J. No. 5)

Rice and cornstarch, at Atlanta, N. Dist. Ga.

Charged 2-3-81: while held by Dah-Tung Trading Co. Inc., Atlanta, Ga., one lot of rice contained rodent filth, and all of the articles had been held under insanitary conditions; 402(a)(3), 402(a)(4). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63317; S. No. 81-288-201; N.J. No. 6)

Salmon, dressed, frozen, at Bellingham, W. Dist. Wash.

Charged 11-17-81: when shipped by Can-Inter-Foods Ltd., Delta, Canada, the article contained decomposed fish; 402(a)(3). Default decree ordered destruction. (F.D.C. No. 63591; S. No. 81-277-869; N.J. No. 7)

Soy flour, at Puerto Nuevo, Dist. Puerto Rico.

Charged 3-2-81: while held by Caribe Storage & Distribution Co. Inc., Puerto Nuevo, Puerto Rico, the article contained insect filth and had been held under insanitary conditions; 402(a)(3), 402(a)(4). Default decree ordered destruction. (F.D.C. No. 63341; S. No. 81-274-856; N.J. No. 8)

FOOD/Economic and Labeling Violations

"Orange juice" concentrate, frozen, at Des Moines, S. Dist. Iowa.

Charged 2-4-82: when shipped by Fresh Pak Foods Inc., Weslaco, Texas, the article, labeled in part "Harrell's frozen concentrated Orange Juice . . . 100% of pure orange juice . . . Valley Citrus Products, Inc. Weslaco, Texas," had had the color turmeric added to it so as to make it appear better or of greater value than it was—402(b)(4); the article contained the non-conforming color additive turmeric, since there was no regulation permitting the addition of turmeric to concentrated orange juice—402(c); the article's labeling was false and misleading in representing the article as concentrated orange juice, since it contained the artificial color turmeric—403(a)(1); the article failed to conform to the definition and standard of identity for frozen concentrated orange juice, since it contained the added color turmeric—403(g)(1); and the article contained the artificial coloring turmeric and its label failed to state that fact—403(k). Default decree authorized donation to a recognized charity for use and not for resale. (F.D.C. No. 63642; S. No. 82-261-871; N.J. No. 9)

COLOR ADDITIVE

"Sorghum" syrup, at Marvel Cave Park, W. Dist. Mo.

Charged 11-3-81: when shipped by Griffin Manufacturing Co., Muskogee, Okla., the article, labeled in part "Lemuel's Pride Old Fashion Home Made Pure Sorghum Lemuel Roye Farms—Stigler, Oklahoma," had had glucose syrup substituted for the article; the article's label was false and misleading in representing that the article consisted wholly of sorghum and that it was manufactured by Lemuel Roye Farms, Stigler, Okla.; the article failed to conform with the definition and standard of identity for sorghum syrup because the article was made with syrup from a source other than sorghum cane—402(b)(2), 403(a)(1), 403(g)(1); the article was also in violation of the Fair Packaging and Labeling Act, since the quantity of contents was expressed in terms of weight instead of fluid ounces followed in parenthesis by a declaration of quarts with any remainder in terms of fluid ounces or fractions of the quart, since the quantity of contents statement was in too small type size, and since the quantity of contents statement was not separated from other printed label information appearing above and below the declaration—15 U.S.C. 1453(a)(3)(A)(i), 1453(a)(3)(C)(i), 1453(a)(2). Default decree authorized donation to charitable institutions for use but not for resale. (F.D.C. No. 63582; S. No. 81-299-234; N.J. No. 10)

Wafer decors, red, at Chicago, N. Dist. Ill.

Charged 3-5-81: when shipped by Richard Girrbach, Wurzbach, West Germany, the articles contained non-conforming color additives, including FD&C Red No. 2, FD&C Red No. 4, and Cochineal Red A; 402(c). Walter Molzahn & Co. Inc., Chicago, Ill., filed a claim to the articles, but did not file an answer to the charge. Subsequently, a default decree ordered destruction. (F.D.C. No. 63324B; S. No. 81-250-155; N.J. No. 11)

DRUGS/Human Use

Faintex ammonia inhalant ampules, and **in-process Faintex aspirin kits (assembled with ammonia inhalant ampules but not yet containing aspirin),** at Framingham, Dist. Mass.

Charged 1-11-80: while held by Stuart Chase Corp., Framingham, Mass., who was in the process of assembling aspirin tablets and ammonia inhalant ampules into kits, the in-process kits and the ampules lacked immediate container labels containing accurate quantity of contents statements, and containing the name and place of business of the manufacturer, packer or distributor—502(b)(1), 502(b)(2); the articles also lacked immediate container labels containing the established name of the active ingredients—502(e)(1)(A). Consent decree authorized release to the dealer for bringing into compliance with the law. Subsequently, the claimant determined that it did not wish to bring the articles into compliance and consented to the destruction of the articles. (F.D.C. No. 62712; S. No. 79-160-267; N.J. No. 12)

Furosemide tablets, sulfamethoxazole & trimethoprim tablets, betamethasone valerate cream, diethylpropion HCl tablets, and **metronidazole tablets,** at Detroit, E. Dist. Mich.

Charged 3-6-81: when shipped by Premo Pharmaceutical Laboratories Inc. (Federal Pharmacal Inc.), South Hackensack, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). Default decree ordered destruction. (F.D.C. No. 63351; S. No. 81-185-259; N.J. No. 13)

Hydroxyzine HCl tablets, at City of Industry, C. Dist. Calif.

Charged 6-5-81: when shipped by Premo Pharmaceutical Laboratories Inc., South Hackensack, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). Consent decree authorized release to the shipper for use in accordance with an effective approved New Drug Application that had been approved after this case had been filed. (F.D.C. No. 63469; S. No. 81-259-482; N.J. No. 14)

Methyl prednisolone acetate suspension (20 mg), at Garner, E. Dist. N.C.

Charged 10-21-80: when shipped by Bel-Mar Laboratories Inc., Inwood, N.Y., the article was a new drug without an effective approved New Drug Application—505(a); and the labeling of the article lacked adequate directions for use and was not exempted due to its new drug status—502(f)(1).

The article was claimed by the shipper. Pursuant to stipulation, the action was transferred to the Eastern District of New York for consolidation with a similar action. Subsequently, a consent decree ordered destruction of all of the 20-mg suspension. (F.D.C. No. 63159; S. No. 80-230-074; N.J. No. 15)

Nitrous oxide, U.S.P., at El Paso, W. Dist. Texas.

Charged 1-26-82: while held by El Paso Welding Supply Co., t/a Border Medical Supply Inc., El Paso, Texas, the circumstances used for the article's processing, packing and holding failed to conform with current good manufacturing practice; 501(a)(2)(B). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63632; S. No. 82-266-690; N.J. No. 16)

Oxygen, U.S.P., at Crystal City, E. Dist. Mo.

Charged 11-28-80: when shipped by Mineweld Inc., Cahokia, Ill., the circumstances used for the article's processing, packing and holding failed to conform with current good manufacturing practice; 501(a)(2)(B). Default decree ordered destruction. (F.D.C. No. 63232; S. No. 80-250-672; N.J. No. 17)

Phenylephrine hydrochloride solution, and **bulk phenylephrine hydrochloride liquid,** at Skokie, N. Dist. Ill.

Charged 5-29-81: while held by Bay Laboratories Inc., Skokie, Ill., who processed the articles using interstate bulk components, the circumstances of the articles' manufacture, processing, packing and holding failed to conform with current good manufacturing practice; 501(a)(2)(B). The articles were claimed by the dealer who denied knowledge about the charge. Subsequently, a consent decree of condemnation ordered the articles destroyed. (F.D.C. No. 63438; S. No. 81-248-327; N.J. No. 18)

Zell H-3 procain HCl, vitamin & enzyme prophylactic tablets, Cyto H-3 procain HCl, vitamin & enzyme geriatric tablets, Phyto-geriatrikum ginseng herb tablets, Zellmedin thymus tablets, Zellkosma vitamin & enzyme liquid, Zellkosma aktiv vitamin & herb cream, Alzym bromelin, paperin, & garlic extract tablets, Vitacain H3 & H7 tablets, and **Wolfmodus tablets,** at San Diego, S. Dist. Calif.

Charged 7-7-80: when shipped by Zellmedin International Ltd., Munich, West Germany, the articles (most of which were labeled in part "Zellmedin International Ltd. . . . Vaduz Consignee: Distribuidora Imperial De B.C. . . . Tijuana, Baja Calif. Norte/Mexico Productos medicinales acc. to order no.") were new drugs without effective approved New Drug Applications; 505(a).

The articles were claimed by Abraham Bautista Yanez, Tijuana, Mexico. The claimant admitted the charges but denied that any jurisdiction existed or that the Federal Food, Drug, and Cosmetic Act had any application to the matter: because the articles had not been shipped in interstate commerce, because the articles had not entered into the commerce of the United States, and because the articles had been shipped in bond, were in transit, and were never offered for entry into the United States (i.e., the entry for transportation and exportation which was covered by the bond had, as the purpose of the bond, the prevention of the entry of the merchandise into the commerce of the United States).

The government moved for summary judgment. The claimant cross-moved for summary judgment. Since the parties had entered into stipulation as to the facts of the action, there were no contested facts and the sole issue over which the parties differed was the question of law: Have the seized articles, shipped as they were from West Germany into the state of California, been shipped in interstate commerce within the meaning of the Federal Food, Drug, and Cosmetic Act? After a hearing on the motions, the court found that the drugs had been shipped within the United States while under bond, and the court ruled in favor of the government.

Upon motion of the government, the court amended its order of summary judgment and findings of fact to add to Finding of Fact No. 4 after the initial phrase "the drugs seized," an additional specification "bonded under 19 U.S.C. §1553." The court's Oct. 21, 1981, amended order for summary judgment read in part:

"This matter came on for hearing on May 4, 1981, on cross-motions for summary judgment. Having heard argument by counsel and having considered the files and records and the pleadings, and being fully advised, the Court makes the following Findings of Fact and Conclusions of Law.

Findings of Fact

"1. The defendant articles under seizure in this case are drugs. 21 U.S.C. §321(g).

"2. The defendants are new drugs. 21 U.S.C. §321(p).

"3. There is neither an approved New Drug Application nor an Investigational New Drug Exemption on file with the U.S. Food and Drug Administration, pursuant to 21 U.S.C. §355, for any of the defendant articles under seizure.

"4. The drugs seized, bonded under 19 U.S.C. 1553, were being transported by air from Munich, Germany, to Los Angeles, Calif., and were en route to Tijuana, Mexico, by land, when detained by the U.S. Customs Service at San Diego, Calif. The seizure was made pursuant to 21 U.S.C. §334.

"5. On July 7, 1980, the United States initiated a civil *in rem* action against the defendant[s], seeking seizure and condemnation.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
5600 Fishers Lane
Rockville, Md. 20857

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"6. Pursuant to a warrant for arrest *in rem* issued by this Court, the U.S. marshal for this District seized the defendant.

Conclusions of Law

"1. This Court has jurisdiction under 21 U.S.C. §334 and 28 U.S.C. §1345.

"2. The seized articles of drug were shipped in interstate commerce from West Germany into California and are now located in San Diego Calif., within the jurisdiction of this Court.

"3. Since the Court finds that the defendant articles of drug are unapproved new drugs, they may not be introduced into interstate commerce, 21 U.S.C. §355(a). Because the defendant articles have been transported in interstate commerce, they are liable to seizure, condemnation and forfeiture, pursuant to 21 U.S.C. §334.

"4. Condemnation under 21 U.S.C. §334 is predicated on a finding that the defendant drugs were in interstate commerce within the meaning of 21 U.S.C. §321(b). The bonding statutes are part of the Tariff Act of 1930, 19 U.S.C. §1001, *et seq.*,and relate exclusively to the appraisement for and the payment of import and export duties. Accordingly, merchandise can be in bond and also in interstate commerce for purposes of the Federal Food, Drug, and Cosmetic Act. The two statutory schemes are not mutually exclusive. *See Archambault* v. *United States*, 224 F.2d 925, 928-929 n.3 (10th Cir. 1955). The Court, therefore, finds that the articles of drug were in interstate commerce and were subject to an enforcement action under the Federal Food, Drug, and Cosmetic Act.

"5. The seized articles of drug may not be brought into compliance with the Federal Food, Drug, and Cosmetic Act because no approved New Drug Application or acceptable Notice of Claimed Investigational Exemption for New Drugs is on file with the FDA. *See United States* v. *Allan Drug Corp.*, 357 F.2d 712, 720 (10th Cir. 1966).

"6. Any Finding of Fact which might be deemed a Conclusion of Law is incorporated in these Conclusions of Law.

"7. There being no genuine issue of material fact, the United States is entitled to summary judgment as a matter of law. It is, therefore, Ordered, Adjudged and Decreed that all drugs under seizure are condemned as unapproved new drugs that have been shipped in interstate commerce (21 U.S.C. §321(p), 21 U.S.C. §355, 21 U.S.C. §334).

"It Is Further Ordered that the U. S. Marshal shall forthwith destroy the condemned goods and make due return to this Court.

"It Is Further Ordered that Claimant shall pay to the United States the costs of such destruction, court costs, and any other proper expenses under 21 U.S.C. §334(e)." (F.D.C. No. 62980; S. No. 80-215-847; N.J. No. 19)

DRUG/Veterinary

Diethylstilbestrol implant pellets, five seizure actions, at Nowata, N. Dist. Okla.; Cordell, W. Dist. Okla.; Houston, S. Dist. Texas; Federick, W. Dist. Okla.; and Guymon, W. Dist. Okla.
Charged 6-18-80, 6-20-80, 9-5-80, 4-1-81, and 4-1-81: while held for sale, the articles were new animal drugs and no approval of a New Animal Drug Application was in effect with respect to their use or intended use; 501(a)(5). Default decrees ordered destruction. (F.D.C. Nos. 63084, 63089, 63110, 63416, 634[illegible]8; S. Nos. 80-211-755, 80-209-945, 80-261-406, 81-266-407, 81-210-352; N.J. No. 20)

MEDICAL DEVICES

X-ray systems, Traceray III, 12 seizure actions, at Windsor, Dist. Colo.; Craig, Dist. Colo.; Battle Ground, W. Dist. Wash.; Portland, Dist. Ore.; Elkhart, N. Dist. Ind.; Tabb, E. Dist. Va.; Milton, N. Dist. Fla.;
Reading, E. Dist. Pa.; Long Beach, C. Dist. Calif.; Louisville, W
Dist. Ky.; Louisville, W. Dist. Ky.; and Mt. Sterling, E. Dist. Ky.
Charged 10-2-79, 10-2-79, 10-16-79, 10-17-79, 10-31-79, 10-9-79, 1
29-79, 10-17-79, 10-5-79 (amended 10-29-79), 10-12-79, 10-12-79 ar
10-31-79: the articles, which had been manufactured by Wester
States Supply Ltd., Pueblo, Colo., were dangerous to health whe
used as directed because the devices would emit radiation beyond th
pre-set exposure time—502(j); the accompanying labeling was fal
and misleading in claiming compliance with the regulation's stan
ards, and in claiming that the devices would deliver the radiatio
exposure stated in the instruction manual—502(a) ; and the article
quality fell below their purported quality—501(c). Consent decre
authorized release to owners/possessors for reconditioning. (F.D.
Nos. 62531, 62532, 62562, 62577, 62597, 62581, 62582, 62584, 6259
62623, 62626, 62634; S. Nos. 79-195-745, 79-117-597, 79-176-82
79-212-741, 79-119-416, 79-206-832, 79-172-756, 79-204-613, 79-21
324, 79-131-418, 79-131-934, 79-131-575; N.J. No. 21)

X-ray systems, Traceray III, two seizure actions, both at Montgomery, M
Dist. Ala.
Charged 10-18-79 and 10-18-79: the articles, which had been manufa
tured by Western States Supply Ltd., Pueblo, Colo., were dangerou
to health when used as directed because the articles would em
radiation beyond the pre-set exposure time—502(j); the accompan
ing labeling was false and misleading in claiming compliance with th
regulation's standards, and in claiming that the devices would deliv
the radiation exposure stated in the instruction manual—502(a); an
the articles' quality fell below their purported quality—501(c). Co
sent decree authorized release to the possessor for reconditionin
(F.D.C. Nos. 62489/90; S. Nos. 79-158-592/3; N.J. No. 22)

X-ray systems, Traceray III, two seizure actions, at Snow Hill, E. Dist. N.C
and Miami, S. Dist. Fla.
Charged 11-2-79 and 10-10-79: the articles, which had been manufa
tured by Western States Supply Ltd., Pueblo, Colo., were dangerou
to health when used as directed because the devices would em
radiation beyond the pre-set exposure time—502(j); the accompany
ing labeling was false and misleading in claiming compliance with th
regulation's standards, and in claiming that the devices would delive
the radiation exposure stated in the instruction manual—502(a); an
the articles' quality fell below their purported quality—501(c). Co
sent decrees authorized destruction. (F.D.C. Nos. 62480, 62520; S
Nos. 79-163-308, 79-193-807; N.J. No. 23)

X-ray systems, Traceray III, two seizure actions, at Wahpeton, Dist. N. D
and Los Angeles, C. Dist. Calif.
Charged 10-1-79 and 10-5-79 (amended 10-29-79): the articles, whic
had been manufactured by Western States Supply Ltd., Puebl
Colo., were dangerous to health when used as directed because th
devices would emit radiation beyond the pre-set exposure time—
502(j); the accompanying labeling was false and misleading in claim
ing compliance with the regulation's standards, and in claiming tha
the devices would deliver the radiation exposure stated in the instruc
tion manual—502(a); and the articles' quality fell below their pur
ported quality—501(c). Default decrees ordered destruction. (F.D.C
Nos. 62529, 62589; S. Nos. 79-195-866, 79-215-322; N.J. No. 24)

NOTICES OF JUDGMENT on Civil Penalty Actions

Picker del Caribe Inc., Gilberto Arguelles, vice president and general manage
and **Mario Nocera,** service manager, Guaynabo, Dist. Puerto Ric
Charged 4-23-79 in a complaint for injunction and civil penalties: tha
the defendants had been engaged in selling, installing and assemblin
diagnostic X-ray systems and sub-systems; that the defendant
installed a certified positive beam limitation cassette holder into

Radiographic-Fluoroscopic unit at Carolina, Puerto Rico, and the cassette holder failed to function in accordance with the prescribed standard and the required certification was either not issued or was not properly issued—42 U.S.C. 263j(a)(5)(A) or (B); that the defendants installed specified diagnostic X-ray systems and/or major components at St. Croix, Virgin Islands (the corporation as the only defendant), Rio Piedras, Puerto Rico, Ponce, Puerto Rico, and Ponce, Puerto Rico, without the required certification and without reporting the assembly to FDA within 15 days—42 U.S.C. 263j(a)(4), & 263j(a)(5)(A); [paragraph 9] that the defendants (the corporation and Giberto Arguelles only) had installed specified diagnostic X-ray systems and/or major components at Carolina, Puerto Rico, Manati, Puerto Rico, Ponce, Puerto Rico Rio Piedras, Puerto Rico, Humacao, Puerto Rico, Bayamon, Puerto Rico, Carolina, Puerto Rico, Utuado, Puerto Rico (all defendants), Carolina, Puerto Rico, and Santurce, Puerto Rico (all defendants)—42 U.S.C. 263j(a)(5)(A); that the defendants sold or otherwise disposed of a Radiographic-Fluoroscopic unit and cassette holder at Carolina, Puerto Rico, that did not conform to applicable performance standards; and that the defendants were aware of federal requirements respecting the need for positive beam limitations in stationary general purpose radiographic units, and the need to certify and to report the assembly of electronic products to FDA.

The defendants denied the charges, but admitted that, due to a misunderstanding as to the potential application of the relevant statute and regulations to the Virgin Islands, certain X-ray equipment was installed there without providing the required certification and without reporting the assembly to FDA within 15 days; admitted that required FDA forms were not filed within 15 days for the above paragraph 9 installations, although all such forms had been filed before this action had been initiated; and admitted that the method and manner of filing through the corporation's parent corporation in the United States had been consented to by FDA. The defendants also filed a notice of a demand for trial by jury. The government opposed such demand and moved that the court grant the parties time to file simultaneous briefs on the question of whether there was a right to a trial by jury in a suit for money damages and injunctive relief. The court granted the government's motion.

Meanwhile, the government requested the production of documents and served written interrogatories on the defendants. The defendants also requested the production of a number of documents.

On Dec. 27, 1979, the court denied the government's motion to strike the demand for a jury trial, saying:

"On July 12, 1979, defendants filed a Notice of Jury Demand requesting trial by jury of this cause pursuant to Rule 38 of the Federal Rules of Civil Procedure (F.R.C.P.). Plaintiff has moved to strike said demand as to the issues solely concerning the petition for a permanent injunction, alleging this is a claim in equity not entitled to trial by jury. [Footnote: Plaintiff asks in its complaint for the imposition of civil penalties (an action traditionally at law) and for a permanent restraining order against further violations (an action traditionally in equity).]

"Although the Federal Rules have abolished the distinction between law and equity, courts must still refer to the ancient common law distinction to decide whether a case is entitled to a jury trial or should be assigned for court trial. *Kerr-McGee Corp.* v. *Bokum Corp.*, 453 F2d 1067 (CA 10th, 1972).

"It is accepted by both parties that issues common to both legal and equitable remedies must be tried before a jury. See *Beacon Theatres* v. *Westover*, 359 US 500 (1959). Plaintiff contends, however, that there are present in this case distinctive issues solely relating to the equitable claim, which must be tried by the Court.

"In situations like the instant one, the Court must exercise its discretion in order to insure the constitutionally protected right of trial by jury. In *Beacon* v. *Westover, supra*, it was held: 'If there should be cases where the availability . . . of joinder in one suit of legal and equitable causes would not in all respects protect the party seeking equitable relief from irreparable harm while affording a jury trial in the legal cause, the trial court will necessarily have to use its discretion in deciding whether the legal or equitable cause should be tried first. Since the right to jury trial is a constitutional one, however, while no similar requirement protects trial by court, that discretion is very narrowly limited and must, wherever possible, be exercised to preserve jury trial.'

"After inquiring into the allegations of the parties as to the existence, at this stage of the case, of issues exclusively related to equitable relief which should be tried by Court rather than by jury, we have not been able to clearly distinguish those 'solely equitable' issues which plaintiff somewhat scatteredly points out, from the issues ultimately bearing on the imposition of a civil penalty.

"The order for restraint of future violations deeply depends on a positive finding of actual violations [Footnote: We surely could not restrict that which could be found not to be happening.] This finding, in turn, is also the basic one regarding the civil penalties claim, which is to be tried by a jury.

"If this Court were to perceive in subsequent stages of this action any questions bearing exclusively on the granting of the injunction, we would rule accordingly. At this moment, this action is not justified.

Meanwhile, the government had moved for the payment of reasonable expenses incurred by the government, alleging that the plaintiff had failed to attend and proceed with a deposition called by the defendants. The defendants opposed such motion. The defendants served written interrogatories on the government and contemporaneously served a second request for the production of documents.

Subsequently, the parties agreed to settle the matter in lieu of further litigation. The defendants were ordered to pay $17,500 to the government. The complaint was dismissed with prejudice as to all parties, and each party was to bear its own costs. (Inj. No. 889; S. No. 78-157-211 et al.; N.J. No. 25)

Rubinstein Dental Equipment Corp., and **George H. Rubinstein**, president, New York, S. Dist. N.Y.

Charged 5-28-80: that the defendants had been engaged in installing and assembling diagnostic X-ray systems; that the defendants had installed a number of specified diagnostic X-ray systems and their major components; that the defendants failed to issue to the purchaser, within 15 days after each of the specified assemblies, the certification required by law and similarly failed to submit to FDA the assembler reports required by law; and that the defendants were well aware that they were violating the law by their failure to certify and report their assembly/installation of diagnostic X-ray systems and their major components; 42 U.S.C. 263j(a)(5) and 42 U.S.C. 263j(a)(4). The defendants filed an answer denying the charges. Subsequently, the parties entered into a consent judgment resolving all of the charges and dismissing the action with prejudice and without costs to either party. Pursuant to the consent judgment, the defendants paid $10,000 in civil penalties to the government. (F.D.C. No. 62415; P.H.S. No. 7; S. No. 79-140-288 et al.; N.J. No. 26)

Xonics Medical Systems Inc., **Walter S. Robertson**, branch manager, and **Richard T. (Dick) Louis**, branch service manager, Seattle, W. Dist. Wash.

Charged 5-20-81: that the defendants were engaged in the installation and assembly of diagnostic X-ray systems and were required by law to furnish a certificate that the product conformed to all applicable performance standards (i.e., the assembler's certification that he

assembled, installed, adjusted and tested all components in accordance with the manufacturer's instructions); that the defendants were required to report installations of such systems and their certified components to FDA within 15 days of the completion of the installation; that the defendants were required to give notice of every safety defect and to remedy such defect by means of correction, replacement or refunding; that on a number of specified occasions the defendants had failed to report to FDA the assembly of diagnostic X-ray systems and/or certifiable components; that on a number of specified occasions false and misleading assembler's certifications had been issued to purchasers representing that the X-ray systems complied with applicable performance standards when the systems did not comply; that on one specified occasion the defendants failed to issue the required certification; that on one specified occasion the defendants failed to notify FDA of a defective installation; and that on one specified occasion, the defendant had failed to bring a diagnostic X-ray system into compliance; 42 U.S.C. 363j(a)(5)(B), 42 U.S.C. 263j(a)(5)(A), 42 U.S.C. 263j(a)(4), 42 U.S.C. 263j(a)(2), and 42 U.S.C. 263j(a)(2).

The parties consented to a judgment against the corporation for $10,000, and against each individual for $2,500. (P.H.S. No. 2; S. No. 81-212-678; N.J. No. 27)

NOTICES OF JUDGMENT on Injunction Actions

Avi Laboratories Inc., and **Gonzalo Ortiz**, president, Hato Rey, Dist. Puerto Rico.

Charged 2-15-79 (amended on or about 3-1-79) in a complaint for injunction: that the defendants manufactured, processed, packed, labeled, stored, held for sale after interstate shipment of components and distributed various drugs; that the circumstances used for the drugs' manufacture, processing, packing and holding failed to conform with current good manufacturing practice; that FDA's inspections revealed serious continuing deviations from current good manufacturing practice—501(a)(2)(B); that the defendants' Febronal Elixir lacked adequate direction for use, lacked the prescribed warning statement for children under 3 and lacked the prescribed dispensing legend, since the article erroneously bore the prescription legend—502(f)(1), 502(f)(2), 503(b)(4); that the defendants' acetaminophen elixir lacked the U.S.P. required expiration date, and had not been included in the defendants' list with FDA of commercially manufactured and distributed drugs—502(g), 502(o); that the defendants' Yodefan lacked the prescription legend—503(b)(1); that other specified drugs were similarly violative; and that the defendants were aware that their activities were in violation of the law.

A consent decree of permanent injunction enjoined the complained of violations and enjoined continued production and distribution unless and until a number of specified conditions were met. (Inj. No. 881; S. No. 77-83-902 et al.; N.J. No. 28)

General Foods Corp., **Ross Barzelay**, president, **Edward Fencl**, division business manager, **David E. James**, quality assurance director, and **James W. Beno**, facility manager, Fulton, N. Dist. N.Y.

Charged 11-16-77 in a complaint for injunction: that the defendants at their plant in Fulton, N.Y., had been manufacturing, processing, packaging, labeling, holding and distributing in interstate commerce various foods including frozen french-style green beans (both with and without almonds and mushrooms); that the defendants (except the quality assurance director and the facility manager) had been engaged at various warehouses outside the state of New York in the receipt of various foods (including such frozen green beans) after interstate shipment from Fulton, N.Y., and the delivery or proffering for delivery thereof for pay or otherwise; that such frozen french-style
green beans contained Geotrichum mold (i.e., machir
had been prepared and packed under insanitary conditi
inspections disclosed a number of specified insanitary
practices relating to the production of frozen fren
beans; that FDA analyses had revealed the presence
mold in various in-plant samples and in three samp
frozen french-style green beans; that the defendants w
of the condition of the green beans and had been warr
the conditions at their Fulton plant; that the de
responded by stating that the corporation intended ca
ment at the Fulton plant prior to the next fresh green
season and had offered to dispose of the FDA sam
declined to discontinue distribution of all other lots
between Aug. 23 and Sept. 10, 1977; 402(a)(3), 402(a)

The parties entered into a stipulation in which th
without admitting any of the allegations in the compl
cease distribution of the frozen green beans (i.e., lots 7
and agreed not to distribute the beans until the court h
the government's motion for a preliminary injunction.

The defendants moved to dismiss the complaint on th
the court lacked jurisdiction over the subject matter of
and that the complaint failed to state a cause of actio
relief could be granted, since the complaint demonstr
commissioner's failure to establish defect action lev
tolerances, with regard to Geotrichum mold, to serve a
the food processing industry.

The case came on for trial before the court. On Fe
court found in favor of the defendants, saying:

"This is an action commenced by the United State
Food and Drug Administration (FDA), for violation of
the Food, Drug, and Cosmetic Act, 21 U.S.C. §331 . .
ment is primarily seeking to enjoin the shipment of f
style green beans processed and packaged by defen
Foods Corporation at its Fulton, New York facility, be
23, 1977 and September 10, 1977, inclusively. . . . The
claims that the defendants have violated the Food, D
metic Act in two separate and distinct fashions. . .

"The [402](a)(3) charge of adulteration stems from
formed upon five samples of finished product, froze
green beans, three of which were taken by FDA inspect
inspection of the Fulton facility on August 23-25, 19
having been confiscated during a September 9-10, 19
Microscopic examinations of those samples revealed t
all five of Geotrichum mold, commonly known as mac

"The [402](a)(4) violation relates to observations m
inspectors during the August and September inspectio
lar, the (a)(4) charge relates to a visible buildup of gre
vegetable matter on belts and equipment contained with
Fulton processing plant. Samples of that slime taken on
occasions revealed the presence of Geotrichum, or mac
The (a)(4) portion of the Complaint also contains allega
insanitary plant conditions, including inspectors' ob
house and fruit flies within the Fulton facility.

Pre-Trial Motion to Dismiss

"The defendants have moved for dismissal of the Co
under Rule 12(b)(1) of the Federal Rules of Civil Proce
U.S.C., claiming that this Court lacks subject matter jur
Rule 12(b)(6), claiming that the Complaint fails to state
which relief can be granted. The gravamen of the defe
ments in support of dismissal concerns the failure of
establish defect action levels (DAL), or tolerances, w
Geotrichum mold, to serve as guidelines to the food proc

try. The defendants claim that, because the presence of Geotrichum in processed frozen green beans is inevitable and unavoidable to a certain degree, the FDA must establish a DAL below which the presence of Geotrichum in frozen green beans will be tolerated by the FDA under section 306 of the Act, 21 U.S.C. §336. The failure of the FDA to establish such a tolerance, the defendants claim, should result in the Government's not being able to establish good cause for granting the injunction, thereby depriving this Court of subject matter jurisdiction. 21 U.S.C. §332(a). The defendants also contend that such failure to establish DALs for Geotrichum renders FDA actions, such as this, for (a)(3) and (a)(4) violations, based upon the presence of Geotrichum, arbitrary and capricious, thereby requiring that this Court deny injunctive relief based upon the equitable 'clean hands doctrine.'

"As previously stated, the green beans in issue are adulterated, under (a)(3), if they consist in whole or part of any filthy substance. The courts which have had occasion to interpret the word 'filthy' as used in that section, have been unanimous in applying a common, everyday definition, rather than attempting to define it in a scientific or technical sense. . . . Under such a definition, there can be no question, and the defendants do not assert otherwise, that Geotrichum mold fragments constitute filth . . . . Under the terms of the statute, an (a)(3) adulteration violation is proven once the presence in the food of any quantity of filth is established. . . . Moreover, to prove adulteration under (a)(3), it is not necessary for the Government to demonstrate that the food is injurious or unfit for consumption . . . . The problem which arises with regard to adulteration under (a)(3), as well as other portions of the Food, Drug, and Cosmetic Act, is brought into sharp focus by the facts of this case, together with the defendants' legal arguments in support of their motion to dismiss. There can be no question that an expert, armed with the proper equipment, could detect filth in virtually every food marketed. . . .

"The FDA, in fact, seemingly recognizes this as being true, as is evidenced by an article, cited by the defendants, which appeared in the *Federal Register* on September 30, 1977. 42 *Fed. Reg.* 52,814 (1977). Consequently, strict enforcement, by the FDA, of section 402 of the Act would result in the banning of literally all processed foods. . . . In order to ameliorate the hardships which would result from such a literal interpretation, Congress empowered the FDA to use its discretion and decline prosecution for minor violations. . . . The defendants contend that the failure of the FDA to set defect action levels, in order to alert the industry as to under what conditions an (a)(3) violation would be prosecuted, based upon the presence of Geotrichum mold, is unfair, and should result in a dismissal of the present case. In support of this argument, the defendants rely heavily upon language contained in Judge Frank's dissent in *United States* v. *449 Cases Containing Tomato Paste,* 212 F.2d and upon the Seventh Circuit Court of Appeals' opinion in *United States* v. *1,500 Cases More or Less, Etc.*, 236 F.2d 208 (7th Cir. 1956).

"Despite the defendants' assertions to the contrary, the FDA is not statutorily required to establish tolerances, or DALs, with respect to (a)(3) violations. . . . While Congress has apparently mandated that the FDA establish tolerances for poisonous or deleterious substances which are required or unavoidable in the production of food, such regulations relating to adulteration under §402(a)(2) of the Act, 21 U.S.C. §342(a)(2), see 21 U.S.C. §346, there is no like requirement relative to (a)(3) violations. That is not to say that the FDA does not have the authority to enact such DALs with respect to (a)(3) violations. . . .

"The mere enactment of regulations establishing tolerances for filth in foods, below which levels the FDA will not prosecute, does not always alleviate the court's task of deciding whether an (a)(3) violation has occurred. The courts are not bound by such DALs and may well choose to apply a stricter standard than that set by the FDA in any particular instance. . . . In fact, a court is not empowered (in theory) to overlook *any* (a)(3) violation, regardless of what tolerance, if any, has been set by the FDA. *United States* v. *449 Cases, Containing Tomato Paste, supra.*

"The harshness of this result is somewhat lessened by the application of a *de minimis* doctrine, whereby small quantities of filth can be overlooked by a court, especially in circumstances where no applicable DAL is in effect *and* there is no evidence that that quantity found is avoidable through the use of good manufacturing practice, taking into account the state of the industry. . . . In applying a *de minimis* standard, a court must, of necessity, rely heavily upon the testimony of expert witnesses well acquainted with both the food and foreign substance at issue, as well as the state of the industry. See, e.g., *United States* v. *1,500 Cases, More or Less, Etc., supra* at 212. For this reason, it would seem that a motion for dismissal of an (a)(3) violation which is arguably *de minimis* should be denied, so that the Court can have the benefit of such witnesses' expertise in applying the *de minimis* doctrine.

"As previously noted, the defendants argue that it is unfair to allow the FDA to indiscriminately exercise its discretion under 21 U.S.C. §336 in determining when or when not to prosecute for (a)(3) violations, in particular relating to Geotrichum mold, which they assert is an unavoidable component of processed green beans. This argument, one proferred in the context of the equitable clean hands doctrine, could easily be considered as a Constitutional vagueness argument, grounded in the Due Process clause of the Fourteenth Amendment. . . . The vagueness argument fails, however, by virtue of the fact that (a)(3) very clearly prohibits all filthy, putrid or decomposed substances contained in food, and is therefore far from vague. . . .

"The equitable argument based upon the unfairness of the FDA charging (a)(3) violations, where no DALs exist to place the industry on notice as to what levels are acceptable, is somewhat more appealing, and has in fact been accepted, to varying degrees, by some. *United States* v. *449 Cases, Containing Tomato Paste, supra,* at 575 (Frank, J., dissenting); *United States* v. *1,500 cases, More or Less, Etc., supra* at 211. The Second Circuit Court of Appeals majority implicitly rejected this equitable argument in *United States* v. *449 Cases, Containing Tomato Paste, supra,* a case in which Judge Frank issued a dissenting opinion explicitly accepting the position now espoused by the defendants. . . . When weighed against the public health and welfare sought to be protected by Congress through enactment of the Food, Drug, and Cosmetic Act . . . the unfairness to the industry is minimized and should not bar enforcement of the Act.

"This Court therefore denies the defendants' motion to dismiss, finding that this Court does possess subject matter jurisdiction, by virtue of 21 U.S.C. §332(a), and rejecting defendants' equitable clean hands argument. The Court will defer any consideration of the *de minimus* doctrine, as applied in this case, until the evidence presented in the trial is weighed.

The Trial

I. Findings of Fact

"A hearing was commenced before this Court on December 19, 1977, upon the Government's request for preliminary and permanent injunctive relief. . . .

"Defendant General Foods Corporation is a Delaware corporation with its headquarters in White Plains, New York. . . . All of the individual defendants exercise some degree of authority over the operation of the Fulton facility.

"The parties have stipulated that all of the frozen, french-style green beans which were processed at defendants' Fulton facility between August 23, 1977, and September 10, 1977, inclusively, and which are currently within the custody or control of defendant General Foods,

have either been introduced into, and subsequently received after movement in, interstate commerce by General Foods, or have been held in New York State for ultimate introduction into or delivery for introduction into interstate commerce.

"On August 23, 1977, Food and Drug Administration (FDA) Consumer Safety Office Investigator Kathleen Shanahan commenced a routine inspection of the General Foods Fulton, New York, processing plant. Miss Shanahan, an FDA employee since 1966, has held her current position since June, 1976, although as a 'stride intern' from 1973-76, she conducted some FDA inspections, and accompanied FDA inspectors on other- [illegible]e August inspection was only Miss Shanahan's second inspection of a frozen green bean processing facility, the other having been of General Foods' Avon, New York, plant, which, at the time, was reprocessing frozen beans. Miss Shanahan has conducted approximately 125-150 inspections, 25-30 of which were of vegetable processing facilities, 5-10 of which, in turn, involved green beans.

"Miss Shanahan began her inspection with a walk-through of the processing facility which, on that occasion was processing only green beans. Inspector Shanahan noted that unprocessed, raw beans are initially placed in a hopper-like farm box outside the plant. . . . From the hopper, the beans are transported to a 'cluster-buster,' designed to separate the beans, then on to an air cleaner, and finally a washer. The aforementioned production stages take place in an outside production area. The beans are then transported to the inside production area, by conveyor belt, where they enter a stainless steel shaker which feeds the beans into 18 snippers, where the ends are removed. The beans are then conveyed, by a combination of belts and shakers, to a series of graders, or sieves, which sort them by diameter to determine whether they are processed as whole, cut, or french-style beans. All of the belts throughout the process are wet. The water used in the plant is Fulton city water and contains approximately one part per million chlorine.

"In the course of her inspection, when reaching this point in production, Miss Shanahan decided to follow the french-style beans production line. She found that from the graders, those beans enter a blancher which cooks the beans slightly for five to six minutes at 212° F, as measured by Miss Shanahan. From the blancher, the beans are passed through a cooling tank, taken by belt to a shaker, and passed over one of the three inspection belts, at which point human inspectors remove undesirable beans. They are then fed, by shaker, into six french cutters. From the cutters, the beans are taken by water flume to the packaging area where they are placed in cardboard boxes. The beans, other than those to be preserved for later reprocessing, are then passed through a freezing tunnel where they are subjected to freon for fast freezing.

"On the first day of the inspection, virtually all of the belts, in the pre-blanch area, be they metal mesh, plastic coated, or cleated, appeared to Miss Shanahan to be covered with a green, slimelike material, generally measuring between one-sixteenth and one-quarter of an inch in thickness. The slime-like material, which Miss Shanahan distinguished from vegetable residue, was grayish-white underneath the green surface. The slimy material smelled strongly of decaying vegetable matter, a smell which pervaded throughout the entire facility, particularly in the pre-blanch area.

"Miss Shanahan returned on the next day, August 24, 1977, to find that no beans were being processed, and the cleaning crew was working in the pre-blanch area. The condition of the belts had not changed since the day before. Miss Shanahan collected 11 subsamples of the slimy material, 10 of which were from the pre-blanch area, and all taken before production resumed. . . . The parties have stipulated that the integrity of these samples, as well as others taken at a later date, was maintained from collection until testing. . . . On August 24, 1977, Miss Shanahan also collected 24 subsamples of finished product manufactured late on August 23, 1977, and 24 finished product subsamples from the first hour of production on August 24, 1977.

"During the August inspection, Miss Shanahan observed several flies, both of the fruit and house variety, saw pre-blanch beans being shovelled from the floor back onto the belts, and noticed that in general, the conditions post-blanch were substantially better, from a sanitation standpoint, than those in the pre-blanch area.

"Miss Shanahan returned to the Fulton facility for a second inspection in the late afternoon of Friday, September 9, 1977. That date was chosen because clean-up at that plant generally took place on Sunday, so that the inspection would come nearly a full week thereafter. . . . During her inspection of the french line, Miss Shanahan again observed a one-sixteenth to one-quarter inch slime buildup on the belts, in approximately the same degree as before, as well as the odor of decaying vegetable matter in the pre-blanch area, flies especially near the presnipper shaker, and open doors and windows. Miss Shanahan collected 25 subsamples, 23 of the slimelike material and two of water. Of the subsamples taken, all but three were from the pre-blanch area. On September 9, 1977, Miss Shanahan also collected eight subsamples of finished product manufactured between August 23, 1977, the date of the first inspection, and that day. She returned the next day, September 10, 1977, and collected subsamples of finished product manufactured on September 9, and September 5. All subsamples of finished products collected were of frozen french-style green beans.

"The subsamples collected in defendant's Fulton facility by Miss Shanahan were analyzed by FDA chemist Jane Kaminski. The finished product subsamples were tested using a modified version of the filth analysis contained in Chapter 44 of the Association of Official Analytical Chemists Manual. . . . In performing this modified AOAC analysis for filth on the samples of finished product collected by Investigator Shanahan, Miss Kaminski obtained the following results: . . .

Mfg. Date	*Average Count*	*Range*
8/23	55 frag/500 g	46—70 frag/500 g
8/24	107 frag/500 g	81/137 frag/500 g
9/9	194 frag/500 g	108—368 frag/500 g
9/5	32 frag/500 g	16—66 frag/500 g
9/5	500 frag/500 g	133—2146 frag/500 g

"Miss Kaminski also tested the environmental samples collected by Inspector Shanahan during the course of her August and September inspections. For those analyses, portions of the subsamples, which were contained in a formaldehyde solution designed to prevent growth, were placed on a covered slide and qualitatively examined under a 100 x microscope. The chemist then looked for the very characteristic features of Geotrichum, including a feathery texture, crossed walls, and series of at least three branches growing oft the main trunk at 45° angles, with tapered growing ends. The presence of Geotrichum, or machinery mold, was detected in each of the 11 subsamples collected by Miss Shanahan on August 24, 1977, and in all but one, #7, of the subsamples from September 9, 1977.

"Added to the testimony of Miss Shanahan's observations, coupled with the results of tests performed on the samples collected by her, the Government points to two of General Foods' internal documents which seemingly acknowledge the presence of some buildup of green, slime-like material on the Fulton bean processing equipment during the period in issue. . . .

"The defendants called Margaret B. Moore, a group leader in the Fulton plant, as a witness to testify as to plant conditions in August and September of 1977. At that time, there were generally 40 line

inspectors and 12 sanitation personnel working during each shift in connection with the bean processing. Mrs. Moore has never seen a one-quarter inch buildup of slime on the equipment, although she does notice occasional small buildups of slime in the plant. Mrs. Moore saw Miss Shanahan in the plant in September, but does not recall anything extraordinary about that night. Mrs. Moore noted that a putrid odor occasionally exists within the plant, generally when the drains become plugged.

"The only other witness having direct knowledge of the actual conditions existing within the plant during the critical time was Richard L. Hazard, food inspector with the New York State Department of Agriculture and Markets. Mr. Hazard made a routine, unannounced inspection of the Fulton plant on August 18, 1977, at which time fresh and frozen green beans were, he thinks, being processed. The only deficiencies noted by Mr. Hazard involved flaking and peeling paint in the production area, and a one or two inch opening of an over-head door through which rodents or insects could enter. He does not recall seeing any slime buildup, smelling a putrid odor, or observing the presence of any flies. Samples of reprocessed, frozen beans taken by Mr. Hazard tested satisfactorily, although the only test requested by Mr. Hazard was for paint particles.

"This Court finds, based upon the foregoing, that on August 23 and 24, 1977, and once again on September 9, 1977, there was some visible buildup, on food processing equipment at the defendants' Fulton facility, of a green, slime-like substance which when qualitatively analyzed, revealed the presence of Geotrichum.

"Geotrichum, commonly referred to within the food processing industry as machinery mold, also known as dairy mold, oospora and oidium, is one whose spores are generally isolated from soil, sewage, and surfaces of fruits and vegetables growing in the field. Geotrichum is not harmful to humans when consumed in food. In fact, it is intentionally introduced into several types of cheese (Limburger, Camemberti, and Brie) as a curing agent, and as such both live and dead Geotrichum is present in those cheeses as part of the finished products. Geotrichum would be killed when subjected to a blanch of 5-6 minutes at 212° F., such as that utilized by the defendants at Fulton, but the dead mycelium would remain unless otherwise removed. Some, though not all, of the mycelial fragments drop off during post-blanch washing.

"Geotrichum spores enter a plant such as that at Fulton in several manners, though primarily on the raw vegetables delivered for processing. The spores require nutrient, moisture, and a proper temperature to grow into viable mycelium. The liquid exuded from a cut or damaged green bean provides an excellent nutrient for Geotrichum spores. Geotrichum, when present in any quantity in a finished food product constitutes filth.

"When Geotrichum begins to grow, it generally takes 4-[illegible] hours to become visible. As it grows, the mold generally appears gray or white in color, although in a food packaging plant its surface would generally take on the color of the juices flowing from whatever food was being processed at the time. The mold accumulation generally has a slimy texture.

"Geotrichum is virtually unavoidable in a food processing plant, particularly one dealing with green beans. The mold can, however, be controlled through the use of proper routine cleaning supplemented by preventative measures, such as high pressure spray of belts and equipment using a chlorine solution. With proper cleaning, visible mold, together with the putrid odor often accompanying it, can be avoided. The presence of analytical Geotrichum, however, especially in a green bean processing plant, cannot be avoided.

"General Foods does not recognize Geotrichum as an indicator of plant sanitation because the mold grows so quickly and because in a neutral pH atmosphere, such as on green beans, bacteria grows to a greater extent than molds or yeasts. Rather, it relies upon a standard plate count as the best indicator of sanitation, setting, as a standard limit, 100,000 living bacteria per gram. They also test for coliform, with a limit of 500 per gram. *E. Coli* is sometimes checked, and occasionally coagulase positive staphylococci with a limit of 100 per gram. Results of such tests performed by General Foods on August 23 and 24, 1977, and September 5 and 8, 1977, were all well within these established limits, which are in turn well below the average within the industry.

"Just as General Foods does not recognize Geotrichum as an indicator of plant sanitation, the Government's experts do not rely wholly upon plate count as such an indicator, because most of the viable microoganisms in the product are killed during blanch, and would therefore not be detected by the standard plate count method. Thus, while these plate counts are adequate indicators of blanch effectiveness, they fail to detect the presence of nonviable filth, such as dead Geotrichum.

"The Court believes the answer to lie somewhere between the two positions. Standard plate count is certainly an indicator of plant sanitation. So too is the visible accumulation of machinery mold, within the processing facility, particularly on surfaces and equipment within which the product will come into contact. Likewise, the quantity of Geotrichum found in the finished product has some bearing upon plant sanitation. The mere presence of analytical Geotrichum in the facility, however, is not necessarily an indication of insanitary conditions.

"The presence of a few flies within a processing plant such as the defendants' is generally unavoidable. An accumulation of fruit flies, however, can be an indication of the presence of decaying matter.

"The practice of shovelling beans off the floor back onto the conveyor belts is not desirable, but does not constitute a violation of Current Good Manufacturing Practices, at least when confined, as here, to the pre-blanch area.

"The only Defect Action Level (DAL) established with respect to Geotrichum, or slime mold, is 20 percent for crushed and canned pineapple, using a Howard Mold Count method of tabulation. Based upon knowing the volume of the fields counted in the Howard Mold Count, and assuming the presence of one Geotrichum filament in each positive field, defendants' experts calculate a 20 percent Howard Mold Count to be the equivalent of 200,000 mycelial fragments per 500 grams. However, Dr. Eisenberg, a Government witness, demonstrated by empirical analysis, based upon Howard Mold Counts and Cichowicz-Eisenberg tests on identical samples of canned pineapple, shows widely varied results, with an average Howard Mold Count of roughly 19 percent being the equivalent of approximately 1,662 fragments per 500 grams, on an average. Of the 12 samples used in making the comparison, the Howard Mold Counts ranged from 16 percent to 23 percent, and the corresponding Geotrichum counts fell between 127 and 6,843 mycelial fragments per 500 grams.

"In March of 1974, the FDA conducted a HACCP (anagram for Hazard Analysis and Critical Control Points) inspection of the Fulton facilities. Following that rigorous, five-day check of equipment and procedures, the FDA determined that the plant was in compliance with their standards. At the time of the inspection, the Fulton plant was processing mushrooms, and repackaging preprocessed, individually quick frozen (IQF) green beans.

Discussion

A. (a)(4) Violation

"The test most often applied in (a)(4) cases, such as this, is to determine whether or not the food in issue was processed under conditions whereby there is a reasonable possibility that filth contamination could have occurred. . . . Because the purpose of (a)(4) is to prevent contamination, or nip it in the bud, actual contamination of the finished product need not be shown. . . . While actual finished product contamination need not be shown, evidence of it is certainly relevant to an alleged (a)(4) violation. . . . Also relevant is evidence of observations made during inspections of the facilities in issue, provided they are conducted at or about the same time that the product alleged to be adulterated under (a)(4) is manufactured. . . .

"To refute allegations of an (a)(4) violation, a defendant may introduce evidence of routine customs, or business habits, involving established cleanup, sanitation, and maintenance procedures, provided they fall within Rule 406 of the *Federal Rules of Evidence*, Title 28 U.S.C. . . .

"The relevant evidence presented bearing upon the (a)(4) violation boils down to: 1) observations by Miss Shanahan of an accumulation of a green, slime-like material on belts and equipment, especially in the pre-blanch area, samples of which tested positive for the presence of Geotrichum; 2) testimony of Mrs. Moore that neither she, nor any of the girls working under her supervision, would allow such a buildup to accumulate without shutting down production; 3) Mrs. Moore does not recall ever seeing such a buildup of slime on the equipment; 4) Mr. Hazard, a state inspector, failed to observe any buildup of slime during his inspection of August 18, 1977, some five days prior to that of Miss Shanahan; 5) the plate counts resulting from defendants' tests performed on the dates in question showed remarkably low levels of living bacteria, coliform, and *E. Coli;* 6) when producing green beans, General Foods uses 40 line inspectors and a 12-man sanitation crew, with a foreman for every shift; 7) General Foods maintains more stringent sanitation requirements for the post-blanch area than the pre-blanch areas; and 8) General Foods concedes that it does not rely upon Geotrichum as an indicator of sanitation. The defendants urge the relevancy of the fact that, following a rigorous 1974 HACCP inspection of the Fulton facility, the FDA determined defendants' facilities and procedures to be in compliance.

"The Court does not consider the 1974 HACCP inspection to be relevant to the (a)(4) allegations, for the simple reason that from 1974 to 1977 one would expect the conditions at the Fulton facility, and the procedures utilized there, to change, very drastically. What is more, the food processing industry is in a constant state of flux, so that what might have been acceptable in 1974 to the FDA as current good manufacturing practice might, in 1977, be totally unacceptable. Evidence of the state inspection conducted in August of 1977 is, however, very relevant to the (a)(4) charge, it being very close in time to the period involved.

"The analytical presence of Geotrichum in samples of both finished product and residue removed from defendants' equipment is not particularly startling, in light of the overwhelming amount of testimony, from experts called by both sides, that Geotrichum is unavoidable in a green bean processing facility. Moreover, the value of those test results as indicators of plant insanitation is outweighed by the extremely low plate counts recovered by the defendants in August and September of 1977.

"Based upon the evidence presented, this Court does not believe the Government has shown, by a fair preponderance of the evidence, . . . that the frozen french-style green beans in issue were processed under such conditions as to present a reasonable possibility that they could have become contaminated with filth.

B. (a)(3)

"The nature of an (a)(3) violation has been explained in the portion of this opinion relating to the defendants' pretrial motion to dismiss. To briefly recapituiate, the literal language of (a)(3), which proscribes filth in food, in any amount, has been interpreted as being subject to exception, both by virtue of section 306 of the Act, 21 U.S.C. §336, which gives the FDA considerable discretion in deciding when to bring actions, and the judicially-evolved *de minimis* rule, which allows a court to overlook a small amount of harmless filth where there is no evidence of that amount of filth being avoidable within the industry.

"Of the samples of finished product tested by Jane Kaminski, the highest count for Geotrichum found in any one subsample was 2,146 mycelial fragments per 500 grams, or just over one pound. The averages found in each of the five finished product samples were 55, 107, 194, 32, and 500 fragments per 500 grams, with the *maximums* found in each being 70, 137, 368, 66, and 2,146 fragments per 500 grams, respectively. By way of comparison, the 20 percent Howard Mold Count defect action level established for crushed and canned pineapple corresponds to 200,000 fragments per 500 grams, using Dr. Olson's computations. According to Dr. Eisenberg's empirical data, an average crushed pineapple sample with a 19 percent Howard Mold Count, represents an average of 1,662 fragments per 500 grams (with a very wide range of results). According to Dr. Olson's calculations, based upon a number of assumptions concerning the average size and mass of a mycelium of Geotrichum, 2,146 fragments in a 500 gram specimen represents approximately .05 parts per million on a mass-to-mass ratio.

"It must be remembered that the Geotrichum inoculum (spores) come into the processing plant primarily on the raw beans, and are provided an ideal environment for growth by virtue of the liquid exuded when the beans are snipped. Thus, we are dealing with contamination inherent in the raw product itself, rather than filth being introduced into the food from the environment during processing.

"The evidence is overwhelmingly supportive of defendants' assertion that Geotrichum is an unavoidable, albeit controllable, problem in the green bean processing industry. There is little or no evidence whatsoever to show that the levels of Geotrichum discovered in defendants' finished product were avoidable through the use of current good manufacturing practices, as exist within the industry. Finally, it is uncontroverted that Geotrichum, at the levels with which we are dealing, is not harmful when consumed by humans. This Court therefore finds that, while the Geotrichum found in samples of defendants' frozen, french-style green beans constitutes filth, the amount is *de minimis*, and does not therefore constitute an (a)(3) violation.

[Footnote: In reaching this conclusion, this Court does not place any reliance whatsoever upon the failure of the FDA to establish a Defect Action Level for Geotrichum in green beans. Such a DAL would certainly be of benefit to the industry, and the public at large. This Court rejects the notion, however, that the FDA is required to set such a standard, and that FDA enforcement of (a)(3) without such a DAL is unfair.]

IV. Conclusions of Law

"The frozen french-style green beans in issue are not adulterated either under section 402(a)(3) of the Act, 21 U.S.C. §342(a)(3), or §402(a)(4), 21 U.S.C. §342(a)(4). The Government is therefore not entitled to injunctive relief pursuant to section 302 of the Act, 21 U.S.C. §332.

"The Clerk shall therefore enter a judgment in favor of the defendants in all respects."

The government moved to temporarily enjoin the distribution of all the allegedly adulterated beans. However, the court ordered that only 50 cases of beans be withheld from distribution pending disposition of the government's appeal. The Court of Appeals affirmed, without opinion, the decision of the District Court. (Inj. No. 808; S. No. 77-82-914 et al.; N.J. No. 29)

Quality Plus Products Inc., and **Thomas Dean Schmoker,** president, Fort Dodge, N. Dist. Iowa.

Charged 1-24-79 in a complaint for injunction: that the defendants manufactured, packaged, labeled and held for sale after interstate shipment of components, and distributed in interstate commerce various drugs for veterinary use; that the circumstances used for the drugs' manufacture, processing, packing and holding failed to conform with current good manufacturing practice; that sulfaguanidine boluses, nitrofurazone tablets, and furazolidone 50 feed medication were new animal drugs and no approvals of New Animal Drug Applications were in effect with respect to the uses or intended uses of the drugs; that a number of the defendants' drugs differed from their purported strength, and fell below their purported quality; that FDA inspections disclosed a number of specified significant deviations from current good manufacturing practice; that FDA analyses of sulfathiazole boluses, ITA-360 boluses, nitrofurazone tablets, and aspirin boluses found those drugs to be contaminated with sulfamethazine, sulfapyridine, sulfathiazole and/or sulfanilamide; and that the defendants were well aware that their activities were in violation of the law; 501(a)(2)(B), 501(a)(5), 501(c).

A consent decree of permanent injunction enjoined the complained of violations, and enjoined continued manufacturing, unless and until a number of specified conditions were met and all drugs on hand were examined, necessary tests were made, necessary recalls were made, and all such drugs were destroyed or brought into compliance with the law. The firm subsequently resumed operations in compliance with the law. (Inj. No. 873; S. No. 78-149-843 et al.; N.J. No. 30)

NOTICE OF JUDGMENT on Miscellaneous Action

Erythromycin estolate ("ee") capsules, and **FDA refusal to certify certain batches of such drug,** Washington, Dist. Columbia.

Charged 11-19-79 by Barr Laboratories Inc., Northvale, N.J., against HEW Secretary Patricia Roberts Harris, and FDA Commissioner Jere E. Goyan, in a complaint for declaratory, injunctive and mandatory relief: that Barr Laboratories Inc. was engaged in the manufacture and sale of generic prescription drugs, pursuant to FDA authority, including erythromycin stearate and erythromycin ethylsuccinate; that Barr was seeking judicial review of FDA's refusal to certify batches of the prescription antibiotic drug erythromycin estolate ("ee") that had been submitted to FDA and found by FDA to meet all the criteria of the applicable FDA monograph; that FDA's refusal to certify batches of "ee" was based solely upon the belief that (a) the monograph for "ee" should be revoked because the drug allegedly had a higher incidence of certain adverse reactions than other equally effective forms of erythromycin, and (b) that, pending its revocation, new manufacturers of the drug should not be allowed to enter the market but no proceeding to revoke the monograph had been initiated, and FDA continued to certify new batches of "ee" submitted by other manufacturers; that certification of Barr's product would not increase the quantity of "ee" prescribed or dispensed; that the sole effect of FDA's refusal to certify Barr's product was to protect the existing marketers of "ee" from loss of market share and to deprive consumers of the benefits of competition; that "ee" had been marketed since 1958 and had been found efficacious as well as safe by FDA; that, in June 1978, Barr sought FDA's evaluation of a protocol for "ee" to show the bioequivalence of its product (the protocol was approved by FDA in July 1978 and the results of the drug study were submitted to FDA on Feb. 1, 1979); that FDA advised the submission of samples of production-size batches; that Barr manufactured production-size batches, submitted samples and was advised by FDA that laboratory results on those batches looked good; that, at that time, FDA had under consideration the removal of "ee" from the market; that FDA had written the principal manufacturer of "ee" requesting voluntary discontinuance of the marketing of "ee" on the ground that the benefit/risk ratio for "ee" was not as favorable as that offered by other forms of erythromycin but that the manufacturer had declined to discontinue and FDA had continued to certify batches of "ee" from that manufacturer; that FDA continued to refuse to certify Barr's batches of "ee" solely on the ground that it had no legal obligation to issue batch certificates to new manufacturers of an antibiotic when FDA doubted the wisdom of the monograph under which certification was requested—notwithstanding that new batch certificates continued to be issued to manufacturers already on the market; that FDA's refusal violated the FDC Act and regulations, constituted unlawful withholding of agency action, was a breach of duty, was arbitrary, capricious and an abuse of discretion, and a violation of the Administrative Procedure Act; and that Barr would continue to be irreparably injured unless the court would declare that FDA acted unlawfully, and would issue an injunction having FDA certify Barr's "ee."

Pursuant to stipulation, the parties agreed to cross-motions for summary judgment and agreed to a number of material facts on which there was no genuine issue.

On Dec. 13, 1979, the court denied Barr's motion for a preliminary injunction, saying:

"Upon consideration of plaintiff's motion for a preliminary injunction, defendants' opposition thereto, and the entire record herein, including oral argument, the Court enters the following findings of fact and conclusions of law:

"The antibiotic erythromycin estolate ('ee') has been marketed in the United States since 1958. A regulation or 'monograph' approving its safety and effectiveness was promulgated in 1971. The principal manufacturer and marketer of 'ee' is Eli Lilly & Co. The drug also is manufactured and marketed by Danbury Pharmacal, Inc.

"Plaintiff, a corporation engaged in the manufacture and sale of generic prescription drugs, has since January, 1979, sought certificates of approval for batches of 'ee' capsules which it has submitted on appropriate forms to FDA pursuant to 21 U.S.C. §357 and 21 C.F.R. §431. Plaintiff refined its production processes, in conjunction with suggestions and responses from agency officials, and submitted an improved batch for approval in July, 1979. It is not disputed that this batch met prevailing standards of safety and efficacy, yet it was not certified.

"Instead, on August 29, 1979, FDA initiated steps with a view to revoking the prior approval of 'ee' because of its conclusion in light of new evidence that 'ee' no longer met applicable safety standards. The drug had long been known to produce certain adverse side effects, and newer scientific data indicated that 'ee' was no more effective than other, safer drugs. FDA unsuccessfully attempted to secure voluntary discontinuance of marketing by Lilly and Danbury. Thereafter, on December 4, 1979, FDA issued a notice of proposed rulemaking to revoke provisions for certification of adult dosage forms of 'ee,' pursuant to 21 U.S.C. §357(f). The agency had earlier publicized its plan of action in the *FDA Drug Bulletin.* FDA continues to refuse to issue certificates to plaintiff, although it will apparently continue to certify batches of 'ee' submitted by Lilly or Danbury on the ground it is required to provide notice and an opportunity for a hearing before it can remove previously approved versions of the drug from the market.

"In reviewing the application for a preliminary injunction, the factors to be weighed are well established. . . . The Court concludes that it is not sufficiently likely that movant will prevail on the merits. The regulation and the relevant application form ('Form 6') appear to suggest that an applicant in the position of plaintiff need simply meet standards of identity, strength, quality, and purity. The legislative history to 21 U.S.C. §357 suggests, however, that certification of antibiotics through this process is an additional burden which does not supersede safety and efficacy requirements even if these requirements ordinarily are not invoked with respect to applicants in plaintiff's position. . . .

"In particular, FDA makes a substantial argument that the agency is not precluded from re-evaluating the safety and effectiveness of an approved antibiotic drug when that drug is offered by a new manufacturer, and that in doing so it has the authority to require such a manufacturer to demonstrate safety and effectiveness as a condition to certification over and above the requirements of Form 6. . . . It is recognized this may result in inequities between manufacturers and even economic hardship for some; but it is persuasively urged that the Act's purpose is to protect public health, not ensure or enhance equitable economic circumstances. Construing the Act liberally, and according due deference to the agency in light of its mandate, the Court presently believes plaintiff is not likely to prevail on the merits.

"In addition, the overriding public interest in safety favors denial of plaintiff's motion. Although the Court has expressed concern that the FDA has not acted more convincingly to cease certifying Lilly's production of the unsafe drug, the agency has now instituted formal revocation proceedings and is informing the medical community of its position. FDA's refusal to certify a new manufacturer while pursuing the deliberative procedures statutorily required for orderly revocation must not be undermined without more persuasive proof than has thus far been offered.

"Finally, the filing of a summary judgment motion by plaintiff, post-argument, means that the legal issues will receive additional attention in depth and the Court will shortly be able to reach a final decision on the merits if, as indicated, a cross-motion is filed. This accelerated time frame minimizes the prospects of irreparable injury to plaintiff in the interim.

"Accordingly, plaintiff's motion for a preliminary injunction is denied. Any further submissions on summary judgment must conform to deadlines set forth in Rule 1-9 of the Rules of this Court."

On Jan. 21, 1980, the court granted the government's motion for summary judgment and ordered the action dismissed, saying:

"Plaintiff Barr Laboratories, Inc. ('Barr'), a small corporation engaged in the manufacture and sale of generic prescription drugs, brings this action to secure declaratory and injunctive relief from defendants, who are charged with administering the Food and Drug Administration ('FDA'). Plaintiff seeks an order requiring FDA to approve for marketing certain batches of erythromycin estolate ('ee') capsules submitted by plaintiff to the agency on July 19, 1979, and any additional batches of that antibiotic submitted by plaintiff in the future and found to conform to existing regulatory standards, 21 C.F.R. §452.115b (1979). Barr claims that FDA is not authorized to withhold certification, and that even if the agency has such authority the exercise of it in this instance is arbitrary, capricious, and without factual justification in the record.

"Having attempted unsuccessfully to resolve its concerns at the agency level, plaintiff is now properly before this Court. 5 U.S.C. §§702-06. It initially moved for a preliminary injunction, and argument from both sides was heard on December 7, 1979. In an effort to assure expedited treatment and minimize possible injury to its business, plaintiff filed a motion for summary judgment immediately following oral argument. The Court denied the motion for a preliminary injunction while anticipating a fuller treatment of the legal issues through the summary judgment process. Defendants have cross-moved for summary judgment, the issues have been fully briefed, and
the Court finds there are no matters of material fact in d

"The essential facts, unchanged since the Court's Me
and Order of December 13, 1979, are as follows:

"The antibiotic erythromycin estolate has been mark
United States since 1958. A regulation or 'monograph' a
safety and effectiveness was promulgated in 1971. Th
manufacturer and marketer of 'ee' is Eli Lilly & Co. The
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certify batches of 'ee' submitted by Lilly or Danbury on th
required to provide notice and an opportunity for a hear
can remove previously approved versions of the dru
market.

"The critical legal issue joined is one of specific statuto
tion. FDA claims that under Section 507 of the Food
Cosmetic Act, 21 U.S.C. §357, it is not *required* to certify
of a previously approved antibiotic when the agency has
drug is unsafe and has initiated statutory procedures to re
the market. Barr argues that under 21 U.S.C. §357, certif
exclusive means for assuring that an antibiotic meet
efficacy standards. It therefore presses on the Court its vi
certification requirements are established, manufacture
comply with those requirements and may not be asked t
safety or efficacy of the drug itself so long as the certi
effect.

"After careful review of the thorough submissions of
the Court concludes that defendants' view must prevail.
enacted in 1945, furnished specific procedures to gov
market testing of the antibiotic penicillin and its deri
provision was passed in haste, to guard against po
hazards associated with the greatly expanded commerci
of penicillin in a peacetime economy. The need adequat
safe and effective use of penicillin, then the only extant a
a clear and overriding purpose of the legislation. . . .
legislative provisions are therefore to be read against the
of this central objective.

"A court must avoid overly literal statutory reading
bring about results completely at variance with the recog
tive purpose. If such a possibility arises, judicial reliance
history is appropriate in an effort to arrive at a reasona
interpretation. . . . In this instance, the particular wor
may appear to suggest that an applicant in plaintiff's
simply meet standards of identity, strength, quality a
order to have his version of an already certified drug a
approved for marketing. The Committee reports, how

that the expedited approval procedure outlined in §357(a) was not intended to encroach upon the agency's broad duty to make basic determinations as to safety and efficacy. Instead, the certification scheme should be read as imposing an additional control on top of safety requirements first identified seven years earlier in section 505 of the Act, . . . moreover, a literal reading of §357(a) would severely impair FDA's ability to prevent increased distribution of antibiotics which it has determined pose a hazard to public health. Having re-assessed the safety and effectiveness of 'ee,' defendants have in effect concluded that the certification regulation itself is no longer an adequate guarantor for public safety. So long as the revocation proceeding is being vigorously pursued, and in light of the clear remedial purpose of the statute, the Court must not deny the agency the authority to refuse to certify new manufacturers. . . .

"Plaintiff argues further that invoking such authority in these circumstances is arbitrary and capricious, because the potential quantities involved pose no incremental health hazard and promise no substantial proliferation of 'ee' capsules on the market. Even assuming this to be the case, plaintiff has not established that the agency action is arbitrary or without factual foundation. Defendants are exercising the full extent of their statutory powers to minimize and ultimately prevent a threat to public health. In doing so they have taken a discretionary measure while pursuing the deliberative procedures required for orderly revocation. As this is apparently the first such occurrence to arise under §357(a), there can be no showing that the justification invoked is not being uniformly applied. Defendants' action here is not inconsistent with prior practice, an important distinction from the conduct challenged in *Rhodia, Inc.* v. *FDA,* No. 77-1616 (Sept. 18, 1979) (slip op. at 7-9).

"Allowing small manufacturers in Barr's position to market 'ee' capsules would simply postpone the no less difficult decision as to when an additional supply on the market poses incremental health hazards to the public. It also would complicate the administrative task of recalling all outstanding supplies of 'ee' capsules should the certification regulation ultimately be withdrawn. In this context, defendants' decision to withhold all new certifications during the pendency of the revocation process is certainly rational. The scientific evidence adduced in favor of revocation, while not at this time dispositive, provides support in the record for FDA's actions to further its public health mandate. Admittedly some inequity occurs when one manufacturer is prohibited from marketing after it has satisfied the same requirements met by others who continue to sell. This result is attributable not to agency caprice but rather to the structure of the statute itself. Because formal certification entitles manufacturers to the procedural protections of §357(f), the agency is in effect faced with an all-or-nothing choice. Its decision to opt for nothing is not arbitrary or an abuse of discretion. Plaintiff is, of course, free to intervene and participate fully in the revocation proceeding.

"Defendants' motion for summary judgment is hereby granted; plaintiff's motion for summary judgment is denied. The case is dismissed. The Court will, however, consider a renewed application from plaintiff upon a responsible showing that defendants have failed vigorously to pursue revocation proceedings pursuant to §357(f)."

Barr Laboratories Inc. appealed to the U.S. Court of Appeals and moved to vacate the District Court's judgment as being moot because Barr was no longer interested in attempting to market erythromycin estolate capsules, and no longer owned any bulk erythromycin estolate from which additional capsules might be manufactured. Upon consideration of Barr's motion to vacate the District Court judgment, and consideration of the government's response stating no objection, the Court of Appeals granted the motion to vacate and remanded the case to the U.S. District Court to vacate the judgment and to dismiss the complaint. (Misc. No. 568; N.J. No. 31)

Notices of Judgment are given pursuant to section 705 of the Federal Food, Drug, and Cosmetic Act. Notices of Judgment report cases involving seizure proceedings, criminal proceedings, and injunction proceedings. Seizure proceedings are civil actions taken against *goods* alleged to be in violation, and criminal and injunction proceedings are against *firms* or *individuals* charged to be responsible for violations. The cases generally involve foods, drugs, devices, or cosmetics which were alleged to be adulterated or misbranded or otherwise violative of the law when introduced into and while in interstate commerce, or while held for sale after shipment in interstate commerce.

Notices of Judgment are prepared by Food and Drug Division, Office of the General Counsel, HHS.

Published by direction of the Secretary of Health and Human Services.

Arthur Hull Hayes Jr., M.D., *Commissioner of Food and Drugs*
Washington, D.C., July 1, 1982

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Section 705[375] of the Food, Drug, and Cosmetic Act: (a) The Secretary shall cause to be published from time to time reports summarizing all judgments, decrees, and court orders which have been rendered under this Act, including the nature of charge and the disposition thereof.
(b) The Secretary may also cause to be disseminated information regarding food, drugs, devices, or cosmetics in situations involving, in the opinion of the Secretary, imminent danger to health, or gross deception of the consumer. Nothing in this section shall be construed to prohibit the Secretary from collecting, reporting, and illustrating the results of the investigations of the Department.

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"…quality and value…" "…always most informative…" "…thorough research…" "…an excellent, excellent journal…. it's marvelous…"

Those are some of the unsolicited comments made recently about the magazine by representatives of industry, business and a foreign consumer agency and by a radio health commentator.

If you're not a regular subscriber, shouldn't you be?

ABBOTT LABORATORIES
North Chicago, Illinois 60064

The Government Relations office of Abbott Laboratories receives the "FDA Consumer" magazine.

My purpose in writing is to acknowledge the quality and value of this publication, which I view as a most worthwhile service of the FDA to the public. The coverage of food and drug issues is timely and the content comprehensive, factual, clearly presented and written, and altogether quality information.

I wholeheartedly support the "FDA Consumer" magazine and thank you for so well representing the FDA to the consumer.

Victoria Stewart-Shain
Washington Representative

COUNCIL OF BETTER
BUSINESS BUREAUS, INC.
The International Assembly of Better Business Bureaus

Having just finished reading April 1982 issue of FDA Consumer, *I wanted to commend you and your staff on the thorough research that goes into your journal. The publication is frequently used by our office for our subject reports.*

We look forward to receiving FDA Consumer *and wish you continued success.*

Annette E. Cleckner
Special Projects Assistant, Industry Standards Division

CONSUMER AFFAIRS BUREAU
The Consumer Affairs Bureau is an agency of the Queensland Government, operating in the interests of consumers and those who serve them.

We await each edition of FDA Consumer *with interest as the articles are always most informative but, even more importantly from a consumer point of view, are written in an entertaining and low key manner.*

Jan Taylor

ENT FOR 7 DAYS ONLY

they're
FDA Consumer . . .

PROGRAM *The Dr. Gabe Mirkin Show*

STATION *WRC Radio*

CITY *Washington, D.C.*

DATE *April 29, 1982 7:05 P.M.*

SUBJECT *Wax Coating*

DR. GABE MIRKIN: *You're on WRC.*

WOMAN: *We've been following your suggestions of eating more fresh fruits and vegetables. However, we have a question we'd like to ask you. Many of them, such as apples and cucumbers, are covered with wax in order to preserve their freshness. And you wash it and you try to scrape it off with a knife. You dislike peeling it because we think the skins are good for us.*

So, is that wax that is on the apples and the fresh fruit that you buy in the grocery store harmful?

MIRKIN: *Well, as far as we know, the wax that covers apples is completely safe. There's not a reason in the world why you should take off the wax.*

And if you're interested, you can call the Food and Drug Administration and get that particular article on wax and apples. It's marvelous. It goes over why they do it, how they do it, and studies on its safety.

WOMAN: *Well, good. You know, sometimes when you scrape it off with a knife, some of it is white, but others look quite dirty-looking. And you think, "My goodness. What am I having?"*

MIRKIN: *As far as we know, it's completely safe.*

MIRKIN: *Incidentally, the last caller asked about waxing an apple. And the magazine I'm talking about is the February issue of the* FDA Consumer.

Many of you may be tired of being had, having your money stolen from you for nonsensical cures of medical conditions that don't exist, taking your money and giving you nothing back. The Food and Drug Administration does an outstanding job. And if you want to spend $17 a year, you can get the FDA Consumer, *an excellent, excellent journal which reviews the FDA seizures of illegal products. It goes over dirty foods, it goes over many topics, like saccharin and sugar and salt and bread and shining an apple with wax.*

Send $17 to the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402. It's called the FDA Consumer. *And let me do that again. You would write for the* FDA Consumer*—it's a monthly magazine—to the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402, for $17.*

It's marvelous and I would recommend it to everybody.

And for the caller who wondered about waxing an apple, it's the February issue, a complete summary of all the pertinent facts.

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FDA
CONSUMER

VOL. 16 NO. 7 **SEPTEMBER 1982**

Worms That Turn Good Food Into Bad **4**
A number of diseases or ailments are caused by parasitic worms that sometimes find their way into food. These maladies range from mild to serious, and sometimes fatal. But in our modern society such troubles can usually be averted with a little caution.

A Touch of Salt for Food Labels **8**
Regulations proposed by FDA urge food processors to provide useful information about sodium content on labels to enable shoppers to control sodium intake in the individual's or family's diet.

Some Medicine for Toothache . . . But None for Bad Breath **10**
Two panels of experts take a look at ingredients in non-prescription toothache remedies and oral health-care products and find that only a few are safe and effective.

Removing the Dread From Epilepsy **13**
Although there's no known cure yet for this nervous system disorder, victims today don't have to cope with the fear and social stigma they used to, thanks to wider knowledge about the condition and effective drugs that make a more normal life possible.

PUVA's Double Whammy on Psoriasis **18**
A treatment regimen that includes a drug taken orally and a type of ultraviolet radiation on affected skin areas is being used today by some medical specialists to remove the unsightly scales of this age-old affliction. However, it's not a permanent cure and there are some risks.

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If misery loves company, this woeful gentleman should look for a friend who happens to have a non-prescription drug containing oil of cloves. That, says a panel of non-government experts, is the only ingredient safe and effective for relieving a toothache with "persistent throbbing" pain. What else the panel had to say on toothache remedies can be found in Some Medicine for Toothache Pain . . . But None for Bad Breath. *The article begins on page 10.*

Richard S. Schweiker
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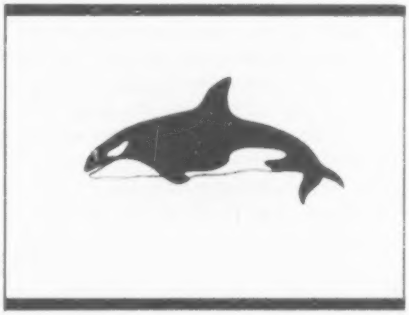

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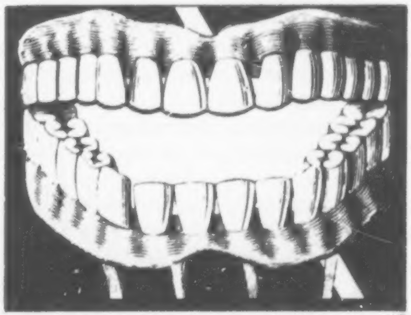


10

Of Lice and Boils

A panel of experts studying the ingredients in non-prescription drugs has come up with good news for people suffering from lice but bad news for those with boils.

The good news is that a non-prescription combination of two pesticides, pyrethrins and piperonyl butoxide, was found safe and effective for treating lice infestations. Neither ingredient, however, was judged effective alone. The ingredients are poorly absorbed through the skin, making them generally safe to use externally. However, people who are allergic to ragweed may have problems with pyrethrins, which come from chrysanthemum flowers and can cause asthma and "hay fever" in allergic persons.

Three varieties of lice attack humans: the head louse, body louse and pubic or crab louse. How the little boogers do their dirty work was described in "All About Cooties and Such Critters" in the December 1980-January 1981 *FDA Consumer*.

The bad news is for boil sufferers. No ingredients in products sold without a doctor's prescription were found effective for treating these skin infections. Further, the panel said, boils should be treated by a doctor because of the risk of a serious blood infection known as septicemia. A boil is caused by an infection of a sweat gland or hair follicle.

These conclusions were made in two reports by the Advisory Review Panel on OTC Miscellaneous External Drug Products. FDA published the reports in the June 29 *Federal Register*, allowing 90 days for interested persons to comment. After the comments are evaluated, the agency will issue proposed standards for both types of products. Once final standards are issued, all non-prescription products for lice and boils must comply with them.

Starch Blockers Questioned

The Food and Drug Administration has asked more than 100 manufacturers and distributors of "starch blockers" to discontinue marketing them until scientific testing confirms the safety and efficacy of these weight management products.

Starch blockers are prepared from raw beans, such as kidney and northern beans, and possibly other, unknown ingredients. The products have been advertised and sold nationwide with claims that they block or impede starch digestion and thus help in weight control and weight reduction by preventing absorption of carbohydrates.

Users of the products have complained to FDA of nausea, vomiting, diarrhea and stomach pains. Persons with diabetes should not depend on starch blockers in calculating their diets.

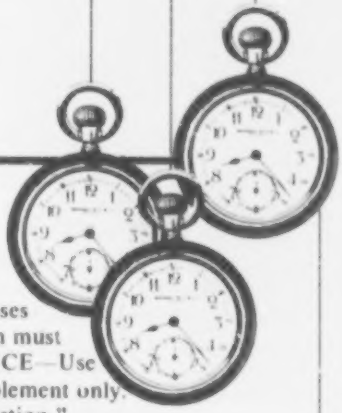
Manufacturers have refused to give FDA specific information about the exact chemical composition of starch blockers. Information supporting claims of safety or effectiveness in weight control or weight reduction has not been provided to FDA. The agency also is concerned about the safety of long-term use of starch blockers, because of the lack of adequate safety testing data.

Some manufacturers assert that starch blockers are special dietary foods. However, because these products claim to control or reduce weight by blocking or interfering with digestion, they may affect the body's normal metabolism function. Under the Food, Drug, and Cosmetic Act, a substance that is offered for a non-food purpose and that alters a function of the body is classified as a drug rather than a food, even if it is derived from a vegetable product.

Manufacturers were given 10 days to stop marketing starch blockers and to provide FDA with information about the manufacture and distribution of these products.

Home for an Orphan Drug?

The substance L-5HTP has been found "valuable" for the treatment of post-anoxic myoclonus, a neuromuscular disease, by the Pharmaceutical Manufacturers Association's Commission on Drugs for Rare Diseases. This was the commission's first evaluation of an "orphan drug"—a product that treats diseases with so few victims that it might go undeveloped without special attention. (Why some drugs are so neglected was explained in "Rx for Orphan Drugs" in the September 1980 issue of *FDA Consumer*.)



The PMA commission announced its findings in June in order to bring them to the attention of potential sponsors of L-5HTP. Such sponsors include pharmaceutical companies, the government, private health organizations and medical research institutions.

Evidence on the clinical use of L-5HTP in myoclonus victims was submitted to the commission by Dr. Melvin H. Van Woert, professor, departments of neurology and pharmacology, Mount Sinai Medical Center in New York City. L-5HTP is a nonpatentable natural substance, presently available only for research purposes.

The commission also recommended development of triethylene tetramine for treatment of Wilson's disease, a condition associated with excessive amounts of copper in body tissues. An approved drug, penicillamine, is available for treatment of this condition, but some patients develop tolerance with prolonged use. Triethylene tetramine is currently under investigation by scientists in private institutions in the United States and the United Kingdom.

Liquid Protein Warnings

FDA has proposed labeling on certain protein diet products to warn that their misuse can be fatal.

The labeling would be required for very low-calorie "liquid protein" diet products such as those linked to a series of deaths in 1977 and 1978, and for other protein powders, capsules and tablets.

Under the proposal, food products deriving more than 50 percent of their calories from protein and promoted for weight reduction would have to carry the following label:

"WARNING: Very low calorie protein diets (below 400 calories per day) may cause serious illness or death. **Do not use for weight reduction without medical supervision.** Not for use by infants, children, or pregnant or nursing women."

Labels or labeling for protein products promoted as part of a nutritionally balanced diet plan providing 400 or more calories would have to declare: "NOTICE—Use only as directed in the diet plan described herewith. Do not use as the sole or primary source of calories for weight reduction."

Food products intended for dietary supplementation that derive more than 50 percent of their calories from protein for purposes other than weight reduction must state on their labels: "NOTICE—Use this product as a food supplement only. Do not use for weight reduction."

The proposed labeling regulation amends a rule that had been scheduled to go into effect in 1980, but was delayed when the U.S. District Court for the District of Columbia questioned certain scientific data related to one of the label statements.

FDA issued a public warning after a government investigation in 1978 found that the deaths of 16 women and one man were associated with the use of protein products in extremely low-calorie diets. Use of these products declined after the warning.

A specially formed U.S. Public Health Service "Protein Diet Task Force" concluded that protein products used as the principal or sole source of nourishment for rapid weight reduction may cause heart irregularities and death.

FDA published the proposed labeling requirements in the June 11 *Federal Register*, allowing 60 days for public comment. If a final rule is published it will become effective 90 days after it appears in the *Federal Register*.

Subscription Price Increased

Once again the Government Printing Office (GPO) has ordered a subscription price increase for *FDA Consumer*. The new price is $21 a year domestic, and $26.25 for foreign subscribers. GPO controls the subscription prices of government magazines such as *FDA Consumer*. GPO sets individual prices according to a formula based on its own expenses. In actuality, GPO provides minimal services to FDA on the magazine, those services being limited to setting up the printing contract for the magazine and handling subscription lists. The Food and Drug Administration pays all other expenses including costs of staff, special graphics, printing and postage. We regret that GPO has decided on this latest price increase—the third in less than 18 months for this magazine—and we hope that you the subscriber will be able to continue to afford the publication.

Worms That Turn Good Food Into Bad

by Marti Asner

Not all worms are found in bad apples. Other fruits and vegetables as well as fish and animals are hosts to such unwelcome guests. So are people.

Unlike the worms discovered in apples, those in many other foods are not often visible in the first bite, nor the last. Often concealed, they exist as microscopic eggs or larvae. If an animal or human eats the infested food, new generations may be produced in an unending cycle. The presence of worms in living hosts and foods may be unknown, subject to detection only by medical probing or laboratory analysis.

In the United States, the human worm burden remains a public health problem, although great strides have been made in sanitation, public education and medical treatment. Even legislation has helped, such as a requirement that garbage fed to pigs be cooked.

Trichinellosis (formerly called trichinosis), which comes mostly from infested pork, is probably the best-known food-borne parasitic disease. But others that cause major health problems around the world are diphyllobothriasis, anisakiasis, heterophyiasis and chlonorchiasis from infested fish; taeniasis from infested beef and pork; and ascariasis and fascioliasis from infested fruits and vegetables (see Table 1).

Trichinellosis is not only the best-known but also one of the most serious of the parasitic worm diseases. The tiny roundworm that produces the disease is called *Trichinella spiralis*. Larval trichinellae infect rats and swine that dine on raw or undercooked meat in garbage. Bears and other wild animals (even the walrus) also may transmit the larvae. Humans can, in turn, become ill after eating undercooked meats from animals that harbor live larvae.

In the stomach the *T. spiralis* larvae (in cysts or "sacs") are undaunted by potent gastric juices and proceed to the intestines. In about 48 hours the larvae mature into adults. Males and females mate and deposit a new generation of *T. spiralis* larvae. Then the moribund parents are evacuated from the body in the feces.

Baby *T. spiralis* larvae bore into the intestinal wall, then travel either to skeletal or heart muscles. Those that reach skeletal muscles dig into the muscle fiber. Life is good to them and they grow into "adolescents" that coil into spiral shapes (thus the specific name "*spiralis*"), develop a protective shell and remain for years. Larvae that enter the heart muscle die quickly; but the lining of this muscle can be seriously injured by even a short stay.

Trichinellosis symptoms vary with individual immunity and the intensity of the infection. During the intestinal phase, a person may experience minor diarrhea. After the *T. spiralis* larvae have invaded the muscle, the victim's symptoms become more severe and may include vomiting, muscular pain, fever, headache, facial swelling, small hemorrhages under the nails and difficulty in breathing. In the severest cases, death may come four to six weeks after onset of the disease.

The U.S. Centers for Disease Control in Atlanta receives about 150 reports a year of trichinellosis cases, of which about one is fatal. CDC suspects that another 100,000 to 300,000 mild cases go unreported. About 25 percent of trichinellosis cases result from eating the flesh of afflicted bears and other wild animals. In 1980 the greatest number of cases were reported in Louisiana (26), New Jersey (24) and Pennsylvania (12). Alaska had only 10 cases but had the dubious distinction of having the greatest rate of cases in proportion to population.

In 1981, an outbreak was reported to CDC involving Asian refugees, many of whom prefer to eat pork lightly cooked. A total of 24 Cambodian and 13 Laotian refugees in Rhode Island contracted the disease after eating raw pork purchased from a local farm. All the patients recovered. In another incident, a 55-year-old woman in Greene County, N.Y., died 19 days after eating raw dried sausage.

Trichinellosis is one of the oldest of known human ills. The Egyptians are credited with developing the first recorded treatment in 1600 B.C. They believed that victims of the disease who ate the bark of the pomegranate tree would evacuate the worms and be cured. This may have worked during the very early stages of the disease. A more modern medication is thiabendazole, used in combination with corticosteroids, to alleviate some of the symptoms.

Prevention is the best safeguard against trichinellosis. To be on the safe side, the U.S. Department of Agriculture advises consumers to cook all pork to a uniform internal temperature of 170 F. Recently the department warned users of microwave ovens that the heat may not be evenly distributed and *Trichinella* organisms may survive in "cold spots." Both USDA and the National Pork Producers Council recommend the following procedures for cooking pork in microwave ovens:

- Choose evenly shaped cuts weighing five pounds or less.
- Cook at low or medium power settings (300 to 350 watts).
- Use a meat thermometer several times to be sure the product is 170 F throughout.
- Rotate the dish several times during cooking.
- Allow meat to set at least 10 minutes after cooking under a tent of aluminum foil. This allows even heat distribution.

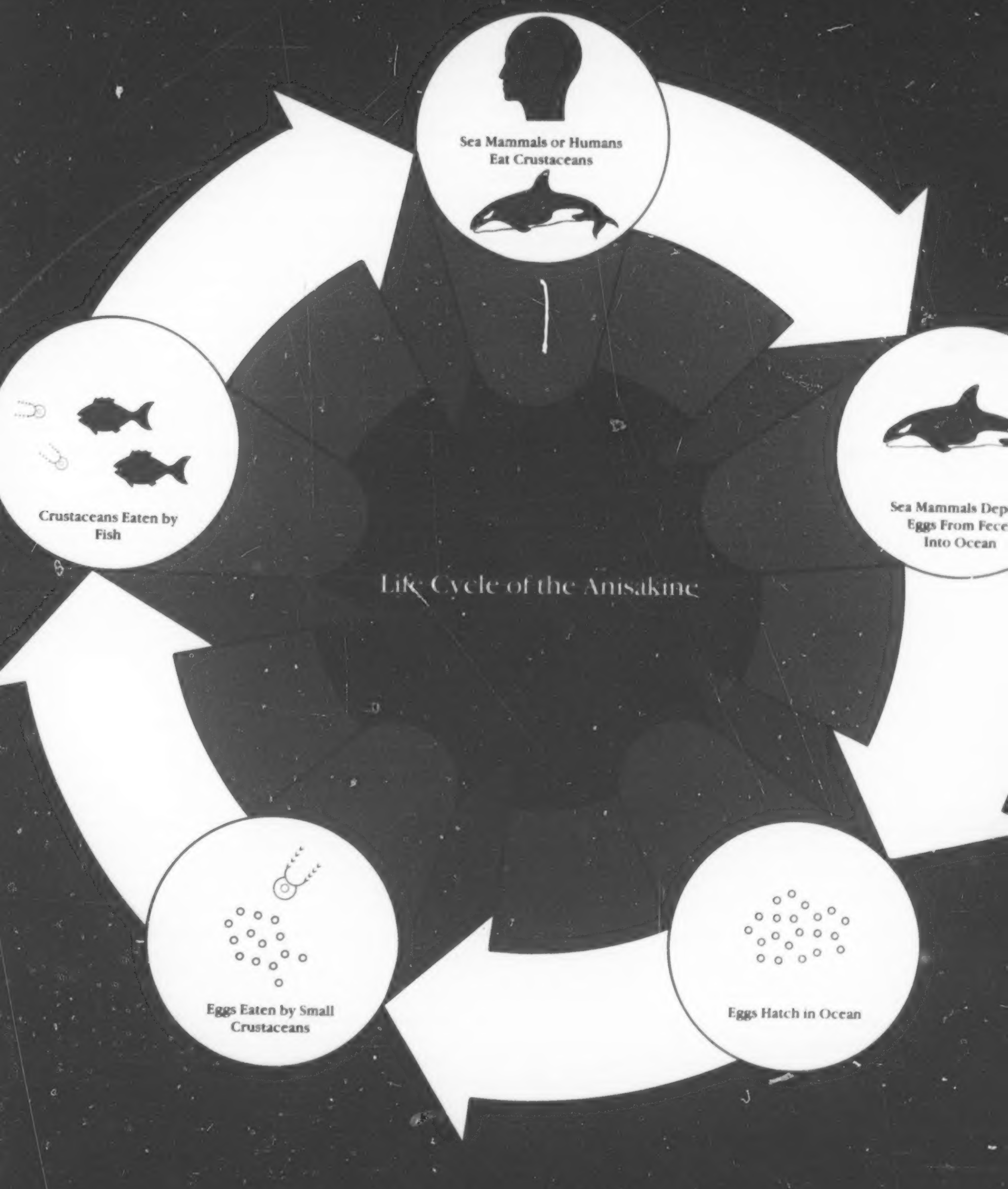

Sea Mammals or Humans Eat Crustaceans
Sea Mammals Dep
Eggs From Fece
Into Ocean
Eggs Hatch in Ocean
Eggs Eaten by Small Crustaceans
Crustaceans Eaten by Fish
Life Cycle of the Anisakine

Figure 1.

Table 1. Examples of Common Food Worm Diseases

Name of Worm	Disease	Source of Illness	Symptoms	Prevention
Trichinella spiralis	trichinellosis	Raw or undercooked meat of infested animals. Found primarily in pork and bear meat.	Vomiting, muscle pain, fever, headache, facial swelling, trouble breathing, small hemorrhages.	Cook all pork and game to a uniform internal temperature of 170 F.
Taenia solium	taeniasis	Infested pork.	In digestive tract: mild diarrhea, false hunger pangs, chronic indigestion. Worms that get into soft tissue may travel to the brain and cause death.	Same as above.
Taenia saginata	taeniasis	Infested beef.	Same as above for digestive tract; does not invade tissues.	Cook beef to an internal temperature of 160 F.
Anisakis species	anisakiasis	Infested marine fish that are raw or undercooked.	Ulcers, hemorrhages, nausea, stomach cramps, granulomas.	Freezing: -4 F for 72 hours. Frying: 140 F for 5 minutes. Baking and broiling: cook until meat flakes easily.
Diphyllobothrium latum	diphyllobothriasis	Infested marine fish that are raw or undercooked.	Usually nonsymptomatic; occasionally abdominal discomfort, nausea, diarrhea, anemia.	Same as above.
Chlonorchis sinensis	chlonorchiasis	Raw or undercooked infested freshwater fish.	Minor liver ailment that may progress to gross liver enlargement, toxic edema.	Same as above.
Heterophyes heterophyes	heterophyiasis	Raw or undercooked infested fish in fresh or brackish waters.	Colicky pains with mucous diarrhea.	Same as above.
Ascaris lumbricoides	ascariasis	Infested fruits and vegetables.	Asthma-like condition, intestinal blockage; can be fatal in children.	Thoroughly wash all fruits and scrub vegetables; canning and long-term freezing.
Fasciola hepatica	fascioliasis	Contaminated watercress.	Fever, abdominal pain, vomiting, jaundice, diarrhea.	If infected sheep are in the area, avoid watercress.

Also potentially life-threatening to humans is the tapeworm called *Taenia solium*, which occurs in countries where people eat undercooked pork. It is rarely encountered in the United States, but it is quite prevalent in certain parts of Mexico and Central Europe. The larvae develop into adults in the small intestine. Some symptoms of the associated illness include hunger pangs, diarrhea and chronic indigestion. Some eggs, which may be consumed in vegetables, hatch in the intestine and the larvae penetrate the digestive tract. If the larvae invade certain areas of the brain, infections can be fatal.

A more common tapeworm in the United States is *Taenia saginata*. The larvae grow in the flesh of cattle and are transmitted to humans in insufficiently cooked or raw beef. Illness symptoms are similar to those caused by *T. solium*, but milder.

Fish lovers also should be cautious when preparing their meals. At least six varieties of worms that can make humans ill are known to infest fish. Most of the fish worm problems in the United States are caused by a group of related roundworms called anisakines. They need three types of hosts to complete their life cycle (see Figure 1). The eggs may occur in the feces of seals, sea lions, whales and other marine mammals. They hatch in the water, and the larvae are eaten by marine invertebrates (small crustaceans), which are then consumed by fish that, in turn, are consumed by marine mammals or humans.

The larvae anchor themselves in the stomach or intestinal lining of the human host, where they can cause ulcers and bleeding. Nausea and stomach cramps are common complaints.

If the worms get restless and start to wander throughout the body, granulomas, or tumors, can appear in the tissues. Such masses are often misdiagnosed as cancerous tumors. Truly adventurous anisakines have been known to roam from the stomach up the esophagus to the throat.

Anisakiasis, like other human worm diseases, is preventable and infestation by this worm is usually not life threatening. Freezing fish at -4 F for 72 hours kills the larvae. Frying temperatures for foods should be at least 140 F for five minutes. There is no specific formula for baking and broiling, but experts recommend cooking the fish until the meat separates easily. There are no drugs currently approved for treatment of this illness.

Diphyllobothriasis, other than a mouthful of syllables, is also a dangerous disease caused by the tapeworm *Diphyllobothrium latum*. The worm behaves in much the same way as the anisakines and may attain lengths to 100 feet in humans. In some cases these tapeworms cause a pernicious anemia in humans. Two years ago this worm caused a rash of human cases on the West Coast, attributed to eating salmon. The type of salmon dish eaten varied. Of the people who became ill, 26 percent had eaten the salmon raw; 41 percent ate only cooked salmon; 7 percent ate it pickled, marinated or salted; and 26 percent ate it prepared in a combination of the previously mentioned methods. (Only one individual ate the salmon at a sushi bar, a Japanese eatery serving raw fish. Sushi chefs, it should be noted, are generally experts in detecting and removing the sac-like larvae and carefully choose deep water fish, which are less apt to be contaminated.) The drug niclosamide has been recently approved by FDA for treating *D. latum* infections.

Another fish worm, the liver fluke, *Chlonorchis sinensis*, is found primarily in the Orient. The worm is transmitted by undercooked, brined or marinated and dried fish. Travelers to the Middle East and Near East should also be aware of a tiny intestinal fluke called *Heterophyes heterophyes*, transmitted in fish, particularly the mullet.

A worm that may infest fruits and vegetables to the detriment of human health is *Ascaris lumbricoides*. *Ascaris* eggs can be found on fresh fruits and vegetables grown in contaminated soil or fertilized with sewage sludge. The worm's eggs survive wherever sanitation is poor and in city sewage systems.

When full size, the *Ascaris* worm resembles the common earthworm. Females can be as thick as a pencil and produce about 200,000 eggs a day. Males are slenderer and are distinguished by an incurved tail. Both sexes are creamy-white with a pinkish hue.

Pesticides, dry weather spells and high humidity do not affect the hard-shelled *Ascaris* eggs. Once swallowed, the eggs hatch in the intestines and the larvae begin a complicated migration through the tissues that lasts up to 10 days.

Symptoms first appear when the larvae reach the lungs. The victim may develop an allergic condition similar to asthma. The larvae then migrate to the small intestine where they mature and remain as adults. An illness caused by a small number of worms may go unnoticed in an adult. Children are especially vulnerable and may suffer intestinal blockage from the worm. In infants, the disease can be fatal. Medication given during the intestinal phase can cause the worm to become more active and to penetrate the intestinal wall, appendix, gall bladder and liver. Eventually, after about two weeks to two months, the worm is expelled in the feces. Drugs used to treat ascariasis include mebendazole, pyrantel pamoate and piperazine citrate.

The best way to prevent ascariasis is to thoroughly wash all fruits in water before eating them and to scrub all vegetables. Canning and long-term freezing also kill the worms.

Not eating watercress in certain areas where sheep are infected is recommended to eliminate the threat of infection by *Fasciola hepatica*, a sheep liver fluke. These organisms are common in contaminated watercress. Infections are more prevalent in Hawaii than in the continental U.S.

No doubt we live in what the eminent worm expert, the late Norman R. Stoll, called "this wormy world." But consumers can protect themselves and their families by taking the necessary precautions when preparing food. After all, what you can't see can sometimes hurt you.

Marti Asner is a member of FDA's public affairs staff.

A Touch Of Salt For Food Labels

by Chris Lecos

Scanning food labels may never be as popular as reading the newspaper funnies. Likewise, the labels on cans of peas and packages of frozen pizza may never be read as thoroughly as the *Daily Racing Form*. However, reading food labels is a lot more popular than reading the old love letters of Attila the Hun.

In fact, since nutrition information was added to food labels nine years ago, it is not uncommon to round a supermarket corner and find a consumer immersed in the facts and figures found on the paper that surrounds a container of food. Since FDA published regulations in 1973 calling on the food industry to start providing consumers with more complete nutrition information, shoppers are able to note the number of calories and the amount of protein, carbohydrate and fat in a specified serving of food. Also available is a listing of the percentages of the U.S. Recommended Daily Allowance (U.S. RDA) of protein and seven vitamins and minerals in a serving.

Nutrition labeling is not used on all food products regulated by FDA and is mandatory only if a food manufacturer adds one or more vitamins, minerals or protein to a product or the labeling makes some kind of nutritional claim about it. But FDA has encouraged the industry to supply nutrition information voluntarily, and many food products today bear this information because the manufacturer is willing to provide it. (Some food products under U.S. Department of Agriculture jurisdiction, such as packaged processed meats, also may carry nutrition labeling.)

Now, through new regulations proposed in the *Federal Register* on June 18, 1982, FDA is urging the food industry to take another major step, primarily on a voluntary basis, to give the American consumer more important labeling information—on the sodium content of food products.

Sodium can be found in measurable amounts in almost every food. There are at least 70 sodium compounds that may be used in food today. FDA's proposed regulations follow a year-long, nationwide campaign of encouraging Americans to reduce their sodium intake and urging the food industry to cut down on the sodium used in food processing. FDA marketing studies indicate that more than three-fourths of the food brands surveyed listed one or more sodium-containing substances in their ingredient lists, attesting to sodium's widespread use in food.

As early as 1904, scientists noticed an association between excessive dietary intake of sodium and high blood pressure, or hypertension. However, it cannot be said with certainty that excess consumption of sodium is what causes high blood pressure.

"Although many epidemiological studies indicate a relationship between sodium intake and the prevalence of hypertension, the evidence that sodium consumption is a major factor in causing hypertension is not fully conclusive," FDA noted. "Nevertheless, the evidence is strong enough for most members of the medical and scientific community to conclude that a substantial portion of the U.S. population which is predisposed to hypertension would benefit from a reduction in dietary sodium."

Hypertension is a leading cause of strokes, and is viewed as a major contributor to heart attacks and heart and kidney failure. It is, said FDA, a "major health concern in the United States today." An estimated 23 to 60 million Americans are believed to be hypertensive.

The main intent of FDA's proposal is to get food manufacturers to identify the sodium content of their products and to establish definitions for the terms "sodium free," "low sodium," "moderately low sodium" and "reduced sodium" used on food labels. Because of possible confusion between the terms "salt" and "sodium," FDA's proposal explains what would be acceptable use of terms such as "no salt added," "salt free" or "unsalted" on the label. Salt and sodium are not synonymous terms. Chemically, salt is sodium chloride. It is about 40 percent sodium and is the largest single contributor of sodium to the human diet.

When the nutrition labeling regulations went into effect in 1973, food producers were not required to include sodium as one of the nutrients on a nutrition label. They were given the option of doing so. By special exemption, a manufacturer also could show the sodium content of a product without having to provide the rest of the required nutrition information. The only mandatory requirement for listing sodium content has been when a food is used or sold for controlling one's sodium intake.

Under the proposed amendments, a food company would have to give sodium content on the label if nutrition labeling is used. It would be listed along with the other required nutrition information. Companies also would be permitted to identify the sodium content without having to use nutrition labeling.

Manufacturers producing foods for special dietary use who want to emphasize lower sodium content would have to follow the criteria set forth in the proposed regulations. They could use these terms on a label, provided certain limits were met:

- The term "sodium free" would refer to any food with 5 milligrams of sodium or less in a specified serving. This would include sodium added to a food and any naturally present. It's possible to detect even minute amounts of sodium in almost any food, but 5 milligrams is considered trivial enough to satisfy the "sodium free" definition. A consumer on an extremely stringent sodium diet could consume 20 servings of "sodium free" food daily with no more than 100 milligrams of sodium.
- The term "low sodium" would apply to foods with 35 milligrams or less sodium in a serving. The National Academy of Sciences National Research Council has estimated that a "safe and adequate intake" of sodium for adults ranges from 1,100 to 3,300 milligrams a day when there is no heavy physical activity or other body demands for more sodium. Thus, 20 servings of "low sodium" foods in a day would keep a person below "normal" levels.
- The term "moderately low sodium" could appear on a label for foods that contain 140 milligrams or less sodium in a serving. Twenty servings at this level would contribute 2,800 milligrams a day.
- The term "reduced sodium" could be used if sodium content is reduced at least 75 percent below that of the regular food item. The label on a reduced sodium product "must bear information comparing the product's sodium content per serving with that of the food it replaces."

In its published comments, FDA acknowledged there is some consumer interest in requiring labeling on certain products indicating they are high in sodium. However, FDA said that imposing such a requirement is not justified at this time because there is "no general scientific agreement on what 'high in sodium' is."

The proposed regulations also would allow foods to be marketed as being "unsalted" or having "no salt added" or some other equivalent phrase provided (1) no salt is added during processing, (2) the food it resembles and for which it is a substitute is normally processed with salt, and (3) the sodium content is stated. A food produced without salt (or sodium chloride) is not necessarily sodium free.

A "salt free" food would be viewed as having false and misleading labeling unless it contained no more than 5 milligrams of sodium in a serving. In effect, it would have to meet the same sodium levels as a "sodium free" product.

After the proposed regulations were published, the food industry, citizen groups and the general public were given 60 days or until Aug. 17, 1982, to submit any comments or reactions to the proposals. A final regulation probably could go into effect sometime in 1983. In publishing the proposals, FDA reiterated its long-standing position that it is relying on voluntary participation by and support from the food industry to achieve the goals of providing consumers not only with more foods in which sodium content is listed but also more processed foods in which the amount of sodium, especially salt, has been cut down. As the agency put it:

"This proposal is the only element in the agency's program that requires a regulation and is not meant to supersede or overshadow the emphasis that FDA places on the voluntary efforts of the food industry." To date, the agency said, FDA has been encouraged by the efforts and interest of the food industry. "Many of the major food companies have advised FDA that they are providing or intend to provide sodium information on their product labels," FDA said. In addition, many food companies are working on ways to reduce the sodium content of their products where feasible. FDA Commissioner Arthur Hull Hayes Jr. has praised the cooperation from industry and has noted that FDA plans to carefully monitor the effectiveness of the present sodium information effort.

Marketing data compiled by FDA gives some indication of the impact the program could have. Based on surveys in 1979 of food brands, 44 percent of packaged food sales in the United States were foods that had full nutrition labeling. Half of the food represented by this sales figure bore nutrition labeling because it was a mandatory requirement; the other half had such labeling because it was voluntary on the part of the manufacturers.

The degree of potential impact can be viewed another way than by sales figures. The 1979 marketing survey involved 1,044 food brands. Of these, nearly 33 percent had nutrition labeling. Fifteen percent of the 1,044 brands bore nutrition labeling because it was mandatory. Thus, under the proposed amendments, at least that number would have to show sodium content if the proposed regulations are approved. Another 17.5 percent of the brands were nutritionally labeled on a voluntary basis, and it is FDA's hope that these, and other products as well, continue to use nutrition labeling including sodium content information.

FDA's 1979 marketing survey also revealed that 1,031 of the food brands listed ingredients on their labels, and of that total, 76 percent included sodium-containing ingredients. Less than 6 percent of these actually gave the amount of sodium. This figure is expected to rise substantially, based on the responses of many food companies to date.

In an evaluation of the economic implications of its proposed regulation changes, FDA concluded that approximately 3,500 food manufacturing firms would incur a first-year cost totaling up to $14.7 million and recurring annual costs of $500,000 to comply with the proposed regulations—costs that would be passed on to consumers. The agency estimated that the first-year cost represented about "one one-hundredth of one percent of consumer expenditures for FDA regulated food products or about three one-hundredths of one percent of consumer expenditures" for all the foods that are nutritionally labeled.

In announcing its proposed sodium labeling regulations, FDA also said it would defer action on the current regulatory status of salt (sodium chloride). Salt is currently considered "generally recognized as safe" as an ingredient in food. Although there are considerable health concerns about the present levels of salt use in the food supply today, the agency said it is "not now proposing any change in the regulatory status of salt . . . because the agency believes that the proposed sodium labeling regulations . . . will respond to those concerns."

Chris Lecos is a member of FDA's public affairs staff.

Some Medicine For Toothache . .

Drugs Take The Bite Out of Toothache

by Annabel Hecht

A few people sometimes have throbbing toothaches. Others wake up in the morning with bad breath. Those with toothaches can get some temporary relief with non-prescription drugs containing oil of cloves (or eugenol). But for those who want to freshen their breath, medical ingredients in mouthwashes may not provide any health benefits and indeed may do some harm.

These are the conclusions reached by two expert advisory panels reviewing the ingredients in toothache remedies and oral health-care products respectively as part of FDA's massive study of the safety and effectiveness of non-prescription, or over-the-counter (OTC), drugs. The reports of the Advisory Review Panel on OTC Dentifrice and Dental Care Drug Products and of the panel on OTC Oral Cavity Drug Products were published by FDA in the May 25, 1982, *Federal Register* to elicit public comment. The recommendations are those of the panel members and are not binding on the agency. After the public comments have been reviewed, FDA will propose standards covering products promoted for non-prescription use for toothaches and for oral health care.

Here is more detail on what the two panels had to say.

There is a consumer population with occasional needs for non-prescription products to treat minor trauma or irritation of the teeth and gums, according to the expert panel on dentifrices and dental care products. Despite the need, the panel found only a few ingredients on the market that are safe and effective for use as (1) agents for the relief of toothache; (2) oral mucosal analgesics (pain-killers); (3) oral mucosal protectants; and (4) tooth desensitizers.

Of the 12 active ingredients in common toothache remedies, only clove oil, or a similar oil containing 85 to 87 percent eugenol (a derivative of cloves), is safe and effective for toothache. But, said the panel, this ingredient should be used only on a tooth with "persistent throbbing" pain. This kind of pain indicates the tooth pulp is already irreversibly damaged, so topical pain-killing products can't cause additional injury, the group reasoned. But if the pain is occasional or intermittent, a characteristic of reversible damage, such products could injure the pulp, perhaps causing irreversible damage, and should not be used.

Three of the 12 ingredients reviewed were not considered safe and effective toothache remedies. They are capsicum (from hot pods of pepper) when used on an open cavity, menthol and methyl salicylate. Further study is needed to determine the safety and effectiveness of nine ingredients, including benzocaine, creosote, phenol and thymol preparations and capsicum as a counterirritant in a poultice that's applied to the gum near the toothache.

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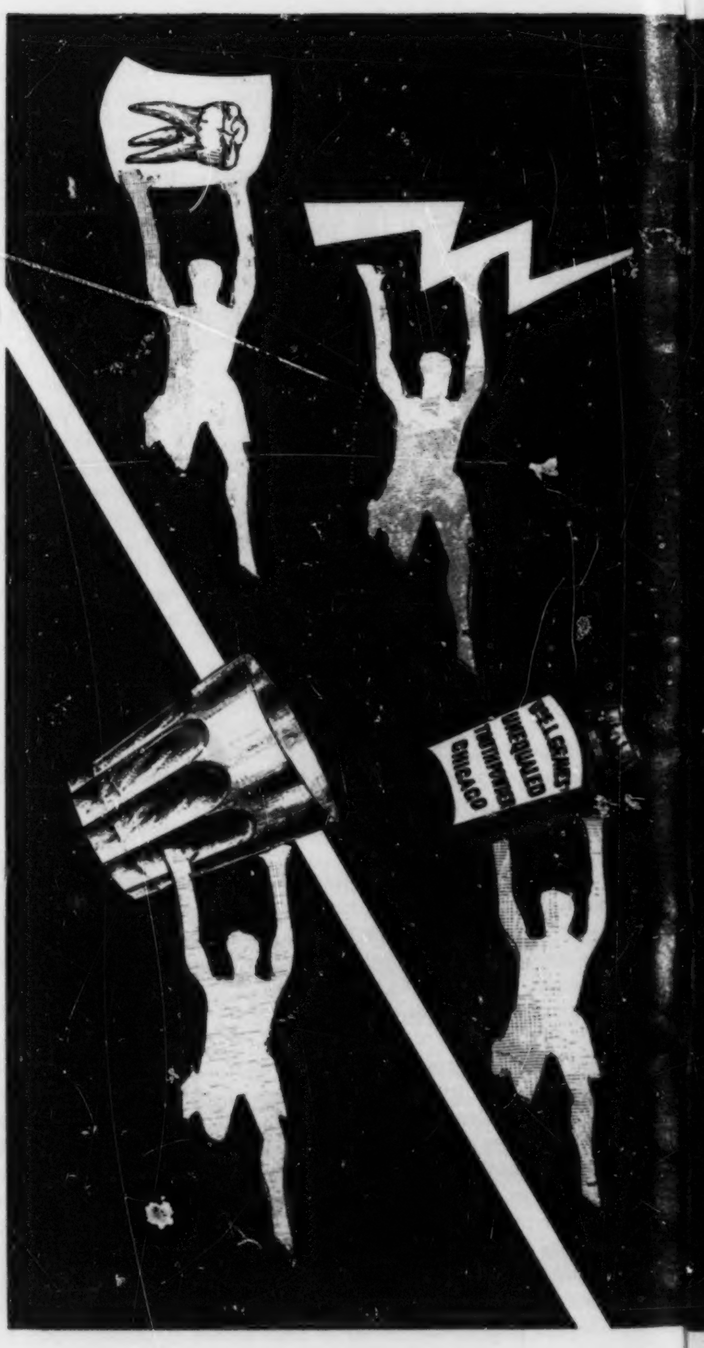
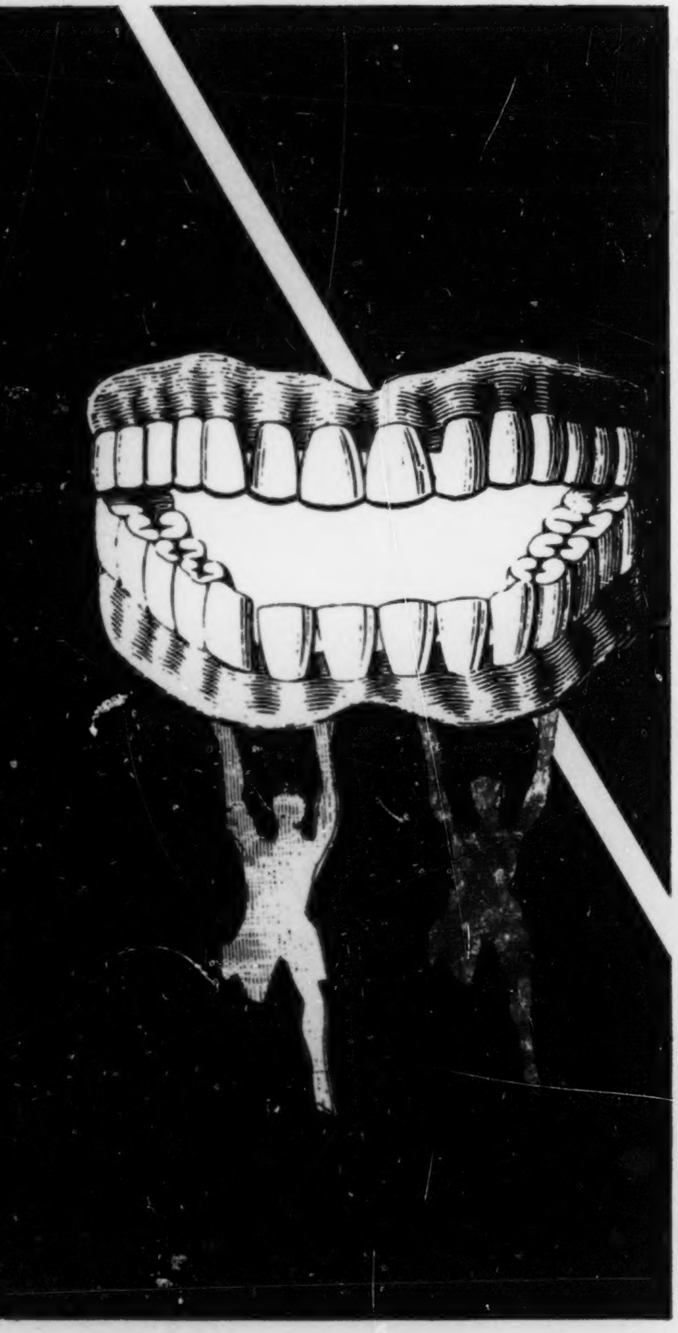


. . But None For Bad Breath

Medicated Mouthwashes Wash Out



Those couples on television who discuss the relative merits of their favorite mouthwash could solve their early morning bad breath problems just as easily by rinsing their mouths with water, brushing their teeth, flossing, or just by eating breakfast, said a panel of experts studying ingredients in oral health-care products.

As for adding germ killers to such non-prescription drugs, the panel vetoed the idea. Bad breath in the morning, something nine out of 10 people have, is not evidence of a systemic or oral disease, the panel said. No health benefits result from the long-term use of antimicrobial agents on a daily basis, and there is evidence that they may be harmful in some instances, the panel said. For these reasons, the panel felt obliged to discourage the use of antimicrobial agents in oral health-care products.

A minority of panel members felt the final report should have included the anti-plaque activity of mouthwashes, which the full panel had considered earlier in its deliberations. In recent years some consumers have used antimicrobial mouthwashes to prevent cavities and periodontal disease by reducing plaque (material that is deposited on the teeth). There have been a number of reports in the dental literature on the clinical effectiveness of three antimicrobial agents in reducing dental plaque, the minority noted.

Nonetheless, the group did classify some 34 active ingredients found in mouthwashes. None, they said, is safe and effective. Ten—including boric acid, ferric chloride, potassium chlorate, sodium dichromate, phenol and cetylpyridinium—should not be used in mouthwashes. Twenty-four ingredients, among them benzoic acid, chlorophyll, eucalyptol, iodine, menthol and tolu balsam, require further tests to determine their safety and effectiveness.

The panel not only discouraged the use of antimicrobial ingredients in mouthwashes but said their labeling should not claim the product kills germs by the millions or in minutes, or inhibits odor-forming bacteria.

The panel also reported on six other categories of oral health-care products: anesthetics/analgesics, astringents, debriding agents, decongestants, demulcents and expectorants.

In the category of anesthetics and analgesics, marketed for the temporary relief of the pain of sore throat, the panel found the following ingredients safe and effective: aspirin benzocaine, benzyl alcohol, dyclonine hydrochloride, hexylresorcinol, menthol, phenol, phenolate sodium and salicyl alcohol. Dyclonine hydrochloride at present is available by prescription only. A minority of the panel members felt aspirin should not be included.

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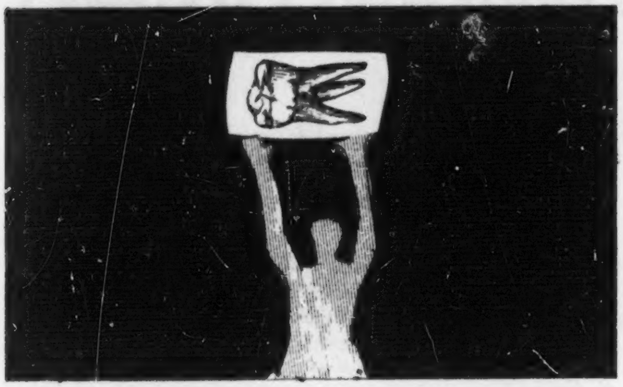

Labeling for toothache remedies should warn that the product is only for persistent, throbbing tooth pain. The user should see a dentist as soon as possible and not use the product for more than seven days, the panel recommended. Toothache products should not be promoted for rapid and effective relief of sore gums or for sore gums following tooth extractions, they said.

Benzocaine, butacaine sulfate and phenol preparations (phenol and phenolate sodium) are all safe and effective as oral mucosal pain-killers, but camphor and methyl salicylate are not, according to the expert panel. Benzyl alcohol and cresol should be further tested.

Oral mucosal pain-killers can be labeled for the temporary relief of pain from minor irritation or injury of soft tissues of the mouth, minor dental work or canker sores already diagnosed by the dentist, the panel said. Labels for products containing benzocaine or phenol can also claim to ease the discomfort of teething in infants and children 4 months of age and older. But, said the panel, these products cannot be labeled as quick acting or especially soothing after extractions or for temporary relief of pain from tooth cavities.

Only two ingredients were reviewed as oral mucosal protectants (substances that help protect irritated areas of the mouth from further irritation from chewing and swallowing). One of them, benzoin preparations (benzoin tincture and compound benzoin tincture), was found safe and effective by the panel, while the other, fluid extract of myrrh, was recommended for further study.

Approved labeling for protectants includes such claims as "forms a coating over a wound" and "protects against further irritation." Labels should warn consumers not to use the product for more than seven days. Unacceptable to the panel are claims such as "especially soothing after extractions or for minor gum boils" or "gives quick relief that lasts for hours."

As for desensitizers, the panel found no ingredients it considered safe and effective to treat hypersensitive teeth, that is, teeth that are extra sensitive to heat and cold. The combination of sodium fluoride, strontium chloride and edetate disodium should not be marketed. Five ingredients, including fluoride preparations, formaldehyde solution and potassium nitrate, should be subjected to additional testing to establish whether they are effective as tooth desensitizers.

(continued from page 11)

Another 10 ingredients were deemed not safe and effective, including antipyrine, camphor, and a number of "caine"-type anesthetics (lidocaine, dibucaine, tetracaine). In addition, eucalyptol, methyl salicylate and thymol should be further tested, according to the panel recommendations.

Oral astringents are drugs that form a thin protective film on the cells of the mouth to lessen their sensitivity to external stimuli. Alum and zinc chloride will do this job, said the expert panel, but tincture of myrrh will not.

Among the ingredients considered as debriding agents (substances that mechanically wash secretions from the surface of the mouth), the panel said carbamide peroxide in anhydrous glycerin, hydrogen peroxide and sodium bicarbonate (baking soda) are safe and effective. Sodium perborate did not measure up as a debrider.

The panel found no ingredients that were safe and effective as decongestants, to aid in the temporary relief of occasional discomfort due to congestion in the mouth and throat. Phenylephrine hydrochloride and phenylpropanolamine hydrochloride might make the grade but first must be subjected to additional testing.

Elm bark, gelatin, glycerin and pectin would be acceptable ingredients in demulcents, according to the panel. Demulcents aid in the temporary relief of minor discomfort and protect irritated areas of the mouth and throat.

Finally, the oral health-care panel said there are no ingredients safe and effective as expectorants to help remove thick secretions from the mouth and throat. They said potassium iodide is not safe and effective and ammonium chloride, horehound and tolu balsam need further testing.

Labeling for all oral health-care products should include a warning that severe or persistent sore throat or sore throat accompanied by high fever, headache, nausea and vomiting may be serious. Such products should not be used for more than two days and should not be given to children under 3 years of age unless directed by a physician. Consumers also should be warned not to swallow these products and to discontinue their use and consult a physician if irritation persists or increases, or a rash appears on the skin.

Among the claims the panel said should not be made are suggestions that the product works quickly, relieves pain from canker sores, helps kill mouth germs, or is soothing and cleansing to the mouth.

Annabel Hecht is a member of FDA's public affairs staff.

Removing The Dread From EPILEPSY

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possible, physicians try to find a single drug that is effective and whose benefits can be balanced against possible side effects or other adverse reactions.

It's estimated that 2.1 million Americans suffer from epilepsy. The three main types of seizures are classified by the Epilepsy Foundation of America as generalized tonic-clonic (or grand mal), generalized non-convulsive (also known as petit mal or absence), and partial. Tonic-clonic is the most dramatic form of epilepsy. As nerve cells discharge throughout the brain the entire body stiffens and shakes, the arms and legs jerk violently, and the victim falls, loses consciousness, becomes rigid and begins breathing irregularly.

Tonic-clonic attacks last one to several minutes. A period of rigidity in the tonic phase is followed by the clonic aspect in which the major muscles alternately contract and relax. As the seizure subsides, a period of deep relaxation follows. Non-convulsive attacks last only a few seconds and consist of blank spells in which the victim loses awareness, twitches slightly, stares and blinks. Unlike tonic-clonic attacks, which are rarely even hundreds of times a day and may even be mistaken for daydreaming or inattentiveness. Partial epilepsy results when nerve cells discharge in a part of the brain, causing a period of mental confusion followed by pointless movements such as pacing and hand rubbing, pain, dizziness and irritability. These seizures can last up to 20 minutes.

There are many less common types, including one in which abnormal electrical activity in a given area of the brain causes spasms in a specific part of the body while the ill person remains conscious. Another less common type causes infantile convulsions in which babies lose consciousness or muscle control for a short while.

Scientists still do not know why neurons build up and discharge in the brain, but epilepsy has been related to birth defects, prenatal damage or injury at birth to the central nervous system, head injuries, poisons, diseases such as measles, circulatory disorders, brain tumors and poor nutrition. In some cases, it is impossible to identify the cause. Those that can be traced to a specific cause are classified as symptomatic; those that cannot are called exactly how medication helps sufferers, but the drugs may work in one or more ways. Some may interrupt the spread of excess energy in the brain while others may increase the amount of a natural seizure inhibitor which turns brain cells on and off like a light bulb. Up to now, therapy has been largely based on experience, but researchers are trying to find better scientific answers that could lead to even more effective treatment.

The physician's skill is especially important in prescribing drugs for the treatment of epilepsy because patients react individually. The right dose needed to gain control of the disease may be determined quickly for some; in others, considerably more experience is necessary before a seizure-preventing level of the drug is reached in the patient's blood. In addition, individuals suffer different side effects from anti-convulsants.

With the development of a technique called anti-epileptic drug level testing, physicians can tell sooner what happens when medication enters a patient's body. This monitoring is carried out by analysis of a blood sample to find the amount of the medication present in the bloodstream, the route by which anti-convulsants reach the areas of the brain where the seizures begin. Levels too low can result in inadequate seizure protection. Levels too high can cause undesirable side effects, including drowsiness or confusion.

Generally, side effects are mild and usually occur at the beginning of therapy. Besides drowsiness or confusion, side effects can include irritability, nausea, rash, some thickening of facial features, increased growth of body hair, some physical clumsiness, overgrowth of gum tissue, and hyperactivity in children. Some individuals undergo emotional changes caused by the drug they are taking. Careful monitoring by the physician is required to customize the proper drug and dosage.

Interaction with other drugs, including non-prescription products, must be watched for and patients are urged to tell their physicians about the other medications they are taking.

Drugs used for treating epilepsy include quinacrine, methsuximide, clonazepam, valproic acid, methamphetamine, dextroamphetamine, acetazolamide, phenytoin, metharbital, chlordiazepoxide, mephobarbital, mephenytoin, primidone, paramethadione, ethotoin, phenobarbital, phenacemide, methylphenidate, carbamazepine, clorazepate, trimethadione, diazepam, and ethosuximide.

The Epilepsy Foundation says that anti-convulsant drugs are successful in preventing seizures in the majority of people who take them regularly and as prescribed. According to the foundation, at least 50 percent of all patients with epilepsy gain complete control of their seizures for substantial periods. For many of this group there may be no seizures for years, while for another 30 percent seizures may be as infrequent as once or twice a month or even once or twice a year, the foundation says.

A recent study published in *The New England Journal of Medicine* reported that certain epileptic children who remain free of seizures during four years of treatment probably can stop taking drugs without suffering relapses. These are children who do not fall into four high-risk categories: (1) those who had epilepsy for a long time before treatment was started, (2) those with mental retardation or physical disability caused by neurological disturbances, (3) patients with certain types of unusual seizures, or (4) those with a combination of seizures.

The study, conducted at Washington University in St. Louis, involved 148 children whose treatment was stopped after four years without a seizure. For up to 23 years afterward only 41, or 28 percent, suffered relapses and these were in at least one of the four risk categories.

Any discontinuance of medication must be carefully monitored by the patient's physician, however, because of the danger of non-stop seizures, which could cause brain damage.

Some patients at all ages continue to experience seizures regularly, even when they take medication, because the right chemical combination has not been found to control their epilepsy. Because of this, researchers are still seeking to produce new drugs and find new ways to use them.

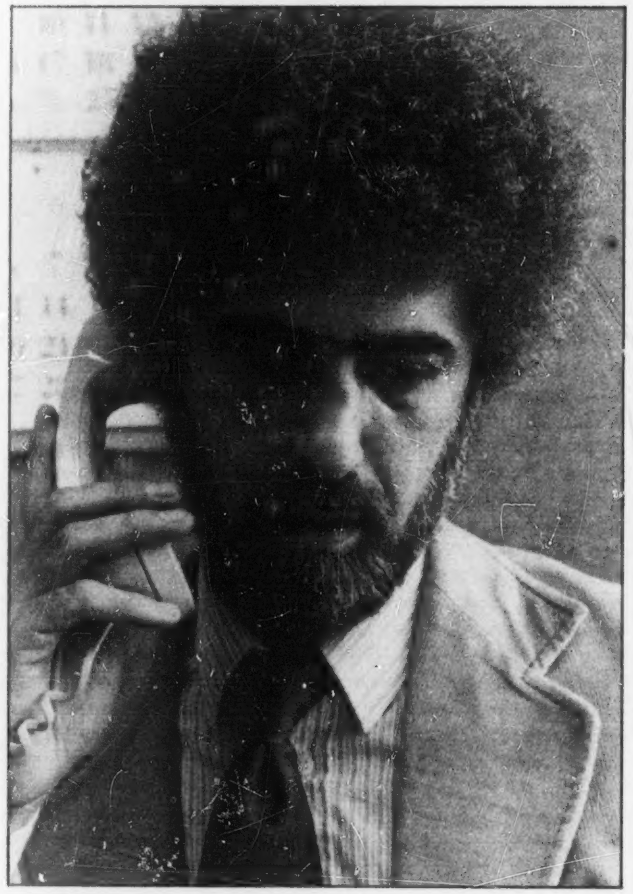
Women who have epilepsy and are also pregnant face a vexing choice between risk and benefit. Without medication there is a risk of having a seizure that could lead to a fall. This might damage the developing child more than a possible fetal defect caused by anti-convulsant medication. There is not enough knowledge for an easy solution to this problem. However, sudden withdrawal of anti-convulsants could cause non-stop, severe seizures that might be injurious to the mother and to the unborn child. The Epilepsy Foundation says that 92 percent of mothers on anti-convulsant medication give birth to normal, healthy babies.

As in other regimens, the patient is a key member of the therapy team. To assist him or her, the Epilepsy Foundation has a publication, *Medication for Epilepsy*, which offers these suggestions for taking medications:

- Don't take less than prescribed. You may have a seizure.
- Don't ever stop your medication abruptly. If you do, you risk a medical emergency in the shape of non-stop seizures that can threaten your life.
- Don't try other people's pills. Even if a friend says he or she has better control with a different medication, check with your doctor instead.
- Don't mix large amounts of alcohol with your medication. This can be a deadly combination. Both anti-convulsants and alcohol act as depressants, and one may intensify the effect of the other.
- Don't drive when starting a new medication until you know how it affects you. You may be able to function perfectly, or it may make you drowsy at first. Find out before you get behind that wheel.
- Don't assume that if you've missed a few doses of your medication you can then make them up safely by taking them all at once. It doesn't work that way. What you need is a certain amount of medication, taken at regular intervals.
- If you have trouble remembering to take your medication in sequence (this may be necessary if you are taking more than one type of anti-convulsant drug), give your memory some help by counting out each day's supply of pills and storing them in special containers, which you can buy at the drugstore.
- Don't let yourself run out of medication. Set up a schedule for reordering so that it becomes automatic.
- Keep all medication locked up and away from children.

John M. Couric is a writer/editor with FDA's National Center for Drugs and Biologics.

The Story Of An Epilepsy Victim



(Contrary to popular belief, most epileptic victims were not born with the problem. Brain damage, often from a blow on the head, is a more likely cause. Here's the story of how one person became epileptic and learned, at long last, to live with it.)

by Gerald Farber

When I was 13 years old, I played a game that started a nightmare which may never go away.

It all began after baseball practice on Easter Sunday in 1959. Eleven of us got together in the woods behind the elementary school where we could sneak a smoke. That was when one of the boys introduced me to a game called "blackout."

The rules were simple: You squatted down, put your head between your legs, breathed through your mouth quickly and deeply about twenty times, and then stood up and blew on your thumb until you passed out. After a few seconds you regained consciousness.

I watched as one after another of my friends played the game. Everyone regained consciousness within a matter of seconds, although some temporarily lost their coordination and others couldn't move at all for a time. I, too, revived in a matter of seconds. Although I was groggy, I felt fine. However, later that evening I developed a headache that grew more severe with the passing hours. When the headache persisted, I was taken to our doctor for a check-up, but she could find nothing wrong with me.

The following afternoon I had a dizzy spell and fell to the floor. My speech became slurred. Then I was taken to the hospital for tests and observation.

Fluid was removed from my spinal column to determine if there was any abnormality of the brain. In another test, objects were placed in my hands, and I was asked to tell what they were without looking at them. At first I had no trouble doing this, but after a few days the sense of feeling on my left side gradually deteriorated. By the fifth day in the hospital, I could no longer identify objects in my left hand. Within a couple of weeks I lost the feeling in both hands.

The doctor then decided to do a right cerebral arteriogram (a brain X-ray) to determine if my condition was due to any swelling of brain tissue caused by accumulation of blood on the surface of my brain. The arteriogram left me in a coma for five days with fevers exceeding 106 F. Neurologists who were consulted said the game "blackout" had caused small hemorrhages in my brain. Dye from the arteriogram had seeped through these hemorrhages and caused more damage to the surface of the brain and the tissue beneath.

After I regained consciousness, my left side was temporarily paralyzed. In the next four weeks I had convulsive spells, during which I had no bladder control. My speech was extremely slurred and incoherent. This lasted for several months. I also suffered a total memory loss and had to relearn everything, right back to the preschool level.

Some months after coming home from the hospital I began having petit mal seizures, a form of epilepsy characterized by frequent, transient lapses of consciousness and occasional falling. Months later I had Asian flu, which brought on my first grand mal seizure, the type of epilepsy that results in a loss of consciousness. My eyes opened and pulled to the left and I suffered convulsions of the arms and legs. I was put on drug therapy. The barbiturates reduced the seizures but left me in a heavily sedated state.

In the summer of 1961 I was admitted to the National Institutes of Health. I was taken off all medication and given a room equipped with a closed-circuit TV so the doctors could monitor my seizures. More tests were done. In the end the doctors said the brain damage was too deep and nothing could be done.

Getting an education was another nightmare. After I recovered sufficiently from the first onset of seizures I returned to school, but I had to repeat the eighth grade. Now 14, I was over six feet tall and towered over the other students. I was considered the "big dumb kid." I can still hear their laughter and taunts after my first seizure in class. Ninth grade in another school was no better. I was expelled as a result of an incident involving some homework I was trying to finish in a different class. The teacher took the paper and I grabbed it back. She thought I was going to hit her.

I never had a discipline problem before the onset of seizures, but now I resented authority of any kind. I was always rebelling against something.

In the summer of 1962 I was sent to a rehabilitation school in Leesburg, Va. The school was truly beautiful, and I wish I could say that I was a model student, but I wasn't. My hostilities arose from the first day I was there. I would occasionally break the rules and go into town to get away. One day I hitched a ride with a trucker who took me as far as Charlotte, N.C. A state patrolman found me wandering the streets at 3 a.m. and I had to wait in jail until someone from the school came to pick me up. The next morning I ate my last breakfast at the school.

My seizures were so bad at this time that I missed a year of school.

In September 1962, I enrolled in high school. Hardly a week went by without an ambulance being called because I had had a seizure in class, even though I told the staff it would not be necessary if I could just be allowed to rest after the seizure.

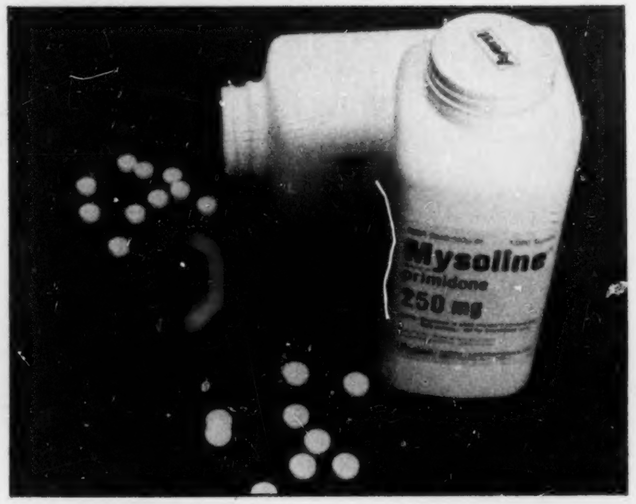
I was 21 when I graduated from high school in 1967. I had always looked forward to graduation and the feeling of succeeding in something nobody thought I could do. I also felt that now a whole new world would open up to me, a grown-up world where people would understand and accept me for what I was and not for what they felt I should be. I was wrong. People were still the same, trying to pretend that I didn't exist or pushing me off into a corner.

After high school I twice went to another rehabilitation school in Fishersville, Va. I started taking a course in general business but couldn't keep up due to my heavy medication.

Job hunting proved to be another nightmare. At interviews I would be told I was just the right man for the job, but when I revealed I was an epileptic there always seemed to be another candidate with better qualifications. I could get work if I didn't mention epilepsy. But this usually lasted only until I had a seizure. Within two weeks I would be fired.

At 22 I started learning various job skills at Goodwill Industries. One day a rehabilitation counselor asked if I would like to work for the federal government. I thought this would be a chance of a lifetime. Shortly after I turned 23, I started working for the Food and Drug Administration. That was in 1969. As a GS-2 clerk, my job wasn't the best in the world, but it was a job.

I had several seizures during my first month there, but nothing was said. Then one day it happened. I had a severe seizure and as I lay on the floor in convulsions, my supervisor said, "I'm going to have to put you out of this office before you hurt yourself." This time I did not walk away. I asked him if he was going to pay my welfare personally or let me try to make a living by working there, even if I did occasionally fall. I asked him not to take away my dignity by telling me I was to be fired because of a seizure.



Every day Gerald Farber must take this medicine to control his epilepsy. But thanks to these tablets, he can lead a normal, productive life.

I stayed on at FDA and eventually was transferred to the press office in the agency's Washington, D.C., offices. Here I am a file clerk and messenger with light typing and other clerical duties. I am pleased to say that I now answer the telephones, something I was not permitted to do at first because my speech was too slow and too slurred due to my medications.

Five years ago I was given a new medication that has left me virtually seizure-free and more alert than I have been at any time since the "accident."

I am now 36 years of age, married and the father of a normal, healthy 6-year-old son and the stepfather of an 18-year-old daughter. Thanks to my medications I am able to lead a reasonably normal life, something I didn't think would ever be possible. Epilepsy is not only a greatly misunderstood condition. It is also a terribly lonely one that imposes isolation, ostracism and rejection on its victims.

My nightmare has subsided now, but it will never end. My seizures are under control, but that does not mean I will never have another one. If the blood tests I must have periodically show deterioration of the bone marrow my medication will have to be changed, with the possibility of more seizures.

I live for the present and future now, but I will never forget my past and how a simple game could so change my life.

PUVA's Double Whammy On Psoriasis

by Larry Bockstahler

PUVA is the acronymal name referring to a fairly new medical treatment intended for severe, stubborn cases of a relatively common skin disorder called psoriasis. The treatment consists of an oral dose of methoxsalen, which makes the skin sensitive to light, and exposure to longwave ultraviolet radiation (so-called UV light).

PUVA gets its name from **P** (for **p**soralen, the class of drug used) plus **UV-A** (an abbreviation for a type of longwave ultraviolet radiation). PUVA therapy was developed by a Harvard Medical School group and was first reported in 1974. Since then it has been tested in cooperative clinical trials at numerous medical centers in the United States and Europe.

The therapy is not a cure for psoriasis; however, it is highly effective in controlling the disease. PUVA was recently approved by FDA on the basis of effectiveness and safety.

Psoriasis is a chronic, recurring skin disease that affects several million people in the United States and 1 to 5 percent of the world's population. Psoriasis comes from the Greek word so spelled, meaning "to have the itch." Psoriasis victims experience an abnormal outer skin layer growth, resulting in red, scaly patches that can occur anywhere on the body. In most cases they occur on the elbows, knees, back, chest, buttocks and scalp. The reddish spots don't hurt and often don't itch. However, they are topped with silvery-white scales of dead skin that are constantly flaking off. The disease is not contagious, but a severe case can be a disfiguring cosmetic problem. The patches and the flaking scales of untreated, severe psoriasis can be embarrassing to victims. Novelist John Updike described what it is like to cope with psoriasis in a short story for the *New Yorker* magazine and in his novel *The Centaur*. Fortunately, most cases are mild, and patients generally are in reasonably good health.

The tendency to psoriasis is inherited but anyone can have it. It is a lifetime disease that may begin at any age, but usually starts early in life. Its cause is unknown.

Everyone sheds some dead skin cells daily, and they are replaced by skin cells that migrate to the surface from deeper layers. Apparently this orderly process is disrupted in people who have psoriasis. The new skin cells multiply too rapidly and form the abnormal patches on the skin's outer layer.

Although psoriasis can't be cured, it is treatable by dermatologists (physicians who specialize in skin problems). A number of conventional treatments exist to remove the symptoms of psoriasis and bring temporary remission. One consists of coal-tar treatment plus exposure to ultraviolet radiation. Millions of dollars a year are spent on these treatments. However, they tend to be messy, inconvenient, time-consuming and expensive.

In PUVA therapy, a patient with severe psoriasis that fails to respond well to conventional treatments might experience something like this:

First comes a discussion of the patient's medical history. Then PUVA therapy would be reviewed, including benefits and potential risks. This may involve a physician who has special competence and training in photochemotherapy, the branch of medicine involving the use of both light and chemicals as "drugs." Once a decision has been made to give PUVA a try, the physician would request that the patient avoid sunbathing for 24 hours before the treatment begins. On the day treatment starts, the drug methoxsalen, also known as oxsoralen or 8-methoxypsoralen, would be given. Methoxsalen belongs to a group of drugs known as psoralens, which are naturally occurring substances found in carrots, celery, parsnips and other vegetables. When eaten, psoralens cause the skin to become much more sensitive to light—especially longwave ultraviolet light. UV light is energy moving through space as invisible waves or particles. It represents that part of the sun's electromagnetic spectrum that lies between visible light and X-rays.

The dose of methoxsalen depends on the patient's weight, among other things. Once the methoxsalen is swallowed (usually with milk or food), it binds to the genetic material (DNA) of the body's cells.

About two or three hours after taking methoxsalen, the patient is exposed to a carefully measured amount of the longwave ultraviolet radiation known as ultraviolet-A, or UV-A. The exposure usually takes place in a specially designed exposure chamber, called a light box or irradiator, with banks of UV-A fluorescent lamps. The patient is asked to remove most or all clothing so as not to inhibit the radiation from reaching the skin. Special goggles must be worn to protect the eyes from damage by the invisible rays. The dosage of UV-A administered depends on several factors such as skin type, previous treatment history and recent exposure to

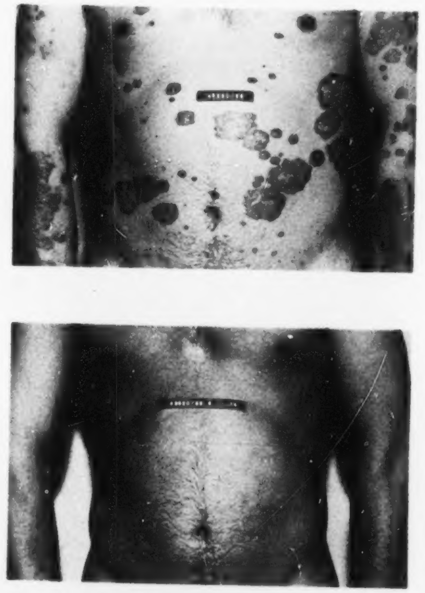
Psoriasis patients take three to six tablets of the drug methoxsalen for each PUVA treatment. Patients are also required to use special goggles for eye protection during the controlled ultraviolet exposure and must wear special glasses before and after treatment to protect against ultraviolet radiation from the sun.

The Curse Of Psoriasis

Had the world been watching, it would have been startled, for my belly, as if pecked by a great bird, was dotted with red scabs the size of coins. Psoriasis. The very name of the allergy, so foreign, so twisty in the mouth, so apt to prompt stammering, intensified the humiliation. "Humiliation," "allergy"—I never knew what to call it. It was not a disease, because I generated it out of myself. As an allergy, it was sensitive to almost everything: chocolate, potato chips, starch, sugar, frying grease, nervous excitement, dryness, darkness, pressure, enclosure, the temperate climate—allergic, in fact to life itself. My mother, from whom I had inherited it, sometimes called it a "handicap." . . .

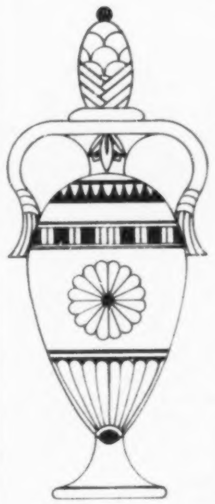
. . . I had come to this conclusion about my psoriasis: it was a curse. God, to make me a man, had blessed me with a rhythmic curse that breathed in and out with His seasons. The summer sun melted my scabs; by September my chest and legs were clear but for a very faint dappling, invisibly pale seeds which the long dry shadow of the fall and winter would bring again to bloom. The curse reached its climax of flower in the spring; but then the strengthening sun promised cure. January was a hopeless time. My elbows and knees, pressure areas of skin, were capped with crust; on my ankles, where the embrace of my socks encouraged the scabs, they angrily ran together in a kind of pink park. My forearms were mottled enough so that I could not turn my shirt cuffs back, in two natty folds, like other boys. Otherwise, when I was in clothes, my disguise as a normal human being was good. On my face, God had relented; except for traces along the hairline which I let my hair fall forward to cover, my face was clear. Also my hands, except for an unnoticeable stippling of the fingernails. Whereas some of my mother's fingernails were eaten down to the quick by what looked like yellow rot.

(From The Centaur *by John Updike, published by Alfred A. Knopf, New York.)*



Typical psoriasis patient, before and after successful PUVA treatments.

(Photos courtesy of Dr. John Parrish, Harvard Medical School.)



PUVA Not So Modern

Sometimes it turns out that the basis of a modern medical treatment is an ancient folk remedy. PUVA therapy is a good example of this. The *Ammi majus* plant, a weed that grows along the Nile River, has been used as a medicinal plant by Egyptian and Indian peoples for centuries. Oil from this plant contains the drug methoxsalen, a compound that makes the skin of humans sensitive to longwave ultraviolet radiation. These ancient peoples found that application of the oil plus exposure to sunlight was successful in treating vitiligo, a skin disorder characterized by white patches of skin cells that lack pigment. This treatment was probably one of the first medical therapies in which light was used as a drug. Nowadays we call such a therapy phototherapy. Therapy such as PUVA, employing the use of both light and a drug, is called photochemotherapy.

sunlight. The first UV-A exposure is usually short, lasting only several minutes. The light penetrates several layers of the methoxsalen-sensitized skin cells. If the treatments are successful, the spread of the disease is halted by inhibition of the growth of new cells in the patches of psoriasis. How and why this happens is unknown. Researchers believe that binding the drug to cellular DNA, followed by UV-A exposure, produces photochemical reactions that somehow inhibit the abnormal growth of new skin cells.

After the UV-A treatment, the patient is given special protective glasses (ordinary sunglasses are inadequate) and asked to avoid sunlight as much as possible over the next 24 hours. More than one PUVA treatment is required, and a regulated schedule is developed for each patient. Usually patients receive two or three treatments a week for a total of 10 to 30 treatments until the psoriasis is cleared. A pinkness of the skin resembling a light sunburn may be noticed after treatment. A tan may even develop.

Periodic PUVA treatments normally are required afterward to keep the psoriasis under control. Many patients must continue the treatments indefinitely to remain cleared.

According to dermatologists, the advantages of PUVA include relative ease of administration, speed of achieving remission and frequent disappearance of psoriasis patches without a trace.

The most common short-term side effects of PUVA therapy that may occur include itching, nausea and skin redness. Painful burns and blistering of the skin can occur if the doses of the drug or the UV-A radiation are excessive or if treatments are too frequent. The margin of safety between effective and toxic exposures of UV-A is narrow.

The most serious potential long-term risk is skin cancer—a risk that sunbathers or sunlamp bathers also take. Follow-up studies made of PUVA patients in U.S. clinical trials at medical centers indicate several times more skin cancer among this group than has been observed in the general U.S. population. The risk was especially greater for patients previously exposed to known potential carcinogens, such as therapeutic X-rays, or those who had had skin cancer.

That PUVA treatments can cause skin cancer is not surprising. It has been shown that methoxsalen can produce skin cancers when applied to the skin of certain laboratory animals and this is followed by exposure to UV-A radiation.

Needless to say, the skin cancer potential is greater for patients who receive maintenance PUVA treatments for many years. Because of the skin cancer threat, PUVA should be avoided altogether by psoriasis patients who have skin that burns instead of tanning, or those who are sensitive to sunlight, have a history of skin cancer, or have received treatment with therapeutic X-rays or arsenic.

Serious eye problems are another potential hazard of PUVA, especially if recommended protective glasses are not used. UV-A radiation penetrates the cornea (outer transparent coat of the eye) and the eye's lens. Exposure to large doses of UV-A causes cataracts to occur in the unprotected eyes of laboratory animals, and the effect is greater if the animals are pretreated with methoxsalen (i.e., PUVA treatment). That's why patients are required to wear protective glasses during and after PUVA treatments. Eye examinations are recommended before therapy starts and every one or two years thereafter.

Premature aging of the skin can also result from PUVA treatment, especially in people who tan poorly.

Larry Bockstahler is a biochemist with FDA's Bureau of Radiological Health.

The Notebook

The Notebook: a potpourri of items gathered from FDA news releases, the Federal Register *and other sources. The* Federal Register *(designated* FR, *with date of publication) is available in many large public libraries.*

■ FDA's newly combined bureaus of drugs and biologics will be called the **National Center for Drugs and Biologics.** The center will have four major offices: new drug evaluation, drugs, biologics, and management.

■ **Drug labeling** regulations may be amended to allow a firm to claim to have made a product actually made by a corporately related firm under common ownership and control. The change was proposed because of concerns that the present rule requiring the corporate name on labels poses problems for certain diversified corporate structures (*FR* June 8).

■ The first **bifocal soft contact lens** to get FDA approval is called Bi-Soft Hydrophilic Contact Bifocal Lens and is a product of the Ciba Vision Care Division of Ciba-Geigy Corp., Atlanta, Ga. The lens is circular with a focus for distance in the center and for close-up vision around the outside.

■ FDA is withdrawing a proposal to halt sales of the antibiotic **erythromycin estolate** (brand name Ilosone) on the recommendation of a special advisory committee. The ban had been proposed because of reports of more incidents of liver damage with its use than with other forms of erythromycin (*FR* May 25).

■ Newport Pharmaceuticals International has withdrawn its request for a hearing on FDA's refusal to approve **Isoprinosine,** used for the treatment of subacute sclerosing panencephalitis (*FR* June 8).

■ Florida residents who received the **snake venom product PROven** in the past may get it on a limited, experimental basis under a license granted to the Miami Serpentarium and the Immunological Research Institute, a new firm, by the Florida Department of Health and Rehabilitative Services. In March, FDA won a court injunction blocking the serpentarium from making PROven and distributing it outside the state because it had not met agency requirements.

■ The administrative record for OTC anti-microbial drug products has been re-opened to allow consideration of an advisory panel's recommendation that **ethyl alcohol and isopropyl alcohol** be classed as safe and effective ingredients in first-aid products to treat minor cuts and scrapes. FDA published a tentative final monograph establishing standards for OTC topical anti-microbial drug products in 1978 (*FR* May 21).

■ COLOR UPDATE: After July 1, 1982, all foods containing **FD&C Yellow No. 5,** the most widely used color additive, will have to identify the color by name on the label. Drugs were required to list Yellow No. 5 after June 26, 1980, and cosmetics have been required to identify this and all other colors by name on the label since May 1976. Some people suffer reactions to the color. . . . FDA is permanently listing **D&C Red No. 30** and **D&C Green No. 5** for use in drugs and cosmetics except those used in the area of the eye (*FR* May 25 and June 4).

■ The use of **formaldehyde** in products FDA regulates is not a threat to public health, the agency says. After receiving a report of a two-year inhalation study on laboratory animals FDA concluded that no regulatory action against use of the substance is necessary at this time. Formaldehyde solution (formalin) is used in various biologicals, human and veterinary drugs, and cosmetics as an inactivating agent, anti-bacterial preservative, or sterilant. It also occurs as an indirect food additive liberated from packaging materials in trace amounts.

■ NOTES FROM THE MARKET BASKET: A National Cancer Institute study has found that **cinnamyl anthranilate** causes cancer in laboratory animals, and FDA has proposed banning its use in foods. The flavoring agent has been used as an imitation grape or cherry flavor in a wide variety of foods, including beverages, ice cream, candy, baked goods, gelatins, puddings and chewing gum. It also has been used as a fragrance ingredient. Since release of the NCI study, industry has informed FDA it has stopped using the agent (*FR* May 25). . . . The food additive regulations are being amended to allow for the safe use of **natamycin (pimaricin)** as a mold-inhibiting agent on surfaces of cuts and slices of cheese where such use is provided for by specific standards of identity (*FR* June 22). . . . FDA is proposing to amend the standard of identity for **canned mushrooms** based on international standards and to amend the standard of fill of container and the drained weight requirements for certain sizes of cans (*FR* June 22). . . . Japan has decided to restrict the use of **potassium bromate,** an additive used in baking, and **butylated hydroxyanisole,** an antioxidant known as BHA, according to an international news source. An advisory council called for the ban because animal tests indicated the additives cause cancer. Neither substance has been banned in other countries.

Willard's Withdrawal Symptoms

by Richard C. Thompson

"As the manufacturer and bottler of Dr. Willard's Water, CAW Industries, Inc. of Rapid City, S.D., does not endorse any claims that its Catalyst Altered Water products are effective in the cure, mitigation, treatment or prevention of any diseases in man or animals. Dr. Willard's Water has not been approved as a 'drug' by the Food and Drug Administration, and CAW Industries, Inc. does not have available scientific proof that its Catalyst Altered Water products are effective in the cure, mitigation, treatment or prevention of any disease in man or animals."

In this short statement, signed April 20, 1982, William J. Willard, president of CAW Industries (and son of the founder), acknowledges that there is no scientific basis for medical claims made over the past 20 years for Willard's Water.

The statement was sent with a cover letter to all distributors of Willard's Water, cautioning them to make no such claims for the product.

Like most products whose sales are based on testimonials, Willard's Water has had a curious history. It was developed by John Wesley Willard, Ph.D., professor of chemistry at the South Dakota School of Mines and Technology at Rapid City, S.D. In the 1930s, he had patented an industrial cleaner for passenger train use that he called "Carbonaceous Activated Water" or "Catalyst Altered Water" (CAW). This basic formulation was reworked over the years and claims for it changed from a simple cleaner to a product that apparently had almost endless uses.

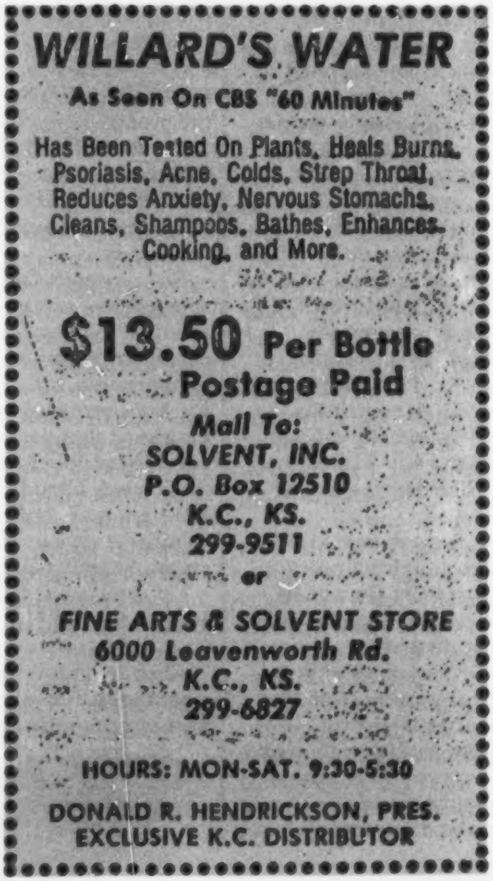
Dr. Willard's Water became widely known in that part of South Dakota among ranchers and townspeople, who were taking it for almost any condition found in man and beast. In 1971 he wrote to FDA, asking about an investigational new drug exemption for Willard's Water that would permit human studies. The agency replied that it needed some additional information, but there is nothing in FDA files to show that Willard followed up on this.

Two years later, Willard formed CAW Industries in Rapid City to manufacture and distribute a second product. That was "Dr. Willard's Water XXX" with lignite, advertised as an aid for plant health and growth. It was to be this product that brought him national attention.

In late 1980, the CBS television program "60 Minutes" featured Willard and his water, showing fruits and plants that were many times their usual size, allegedly because of Willard's Water treatment. In his enthusiasm, Willard told of all the other remarkable qualities of his product and how beneficial it had been to those who had used it. A national sales system quickly formed, with regional and local distributors holding franchises.

Some of these distributors expanded on the virtues of Willard's Water, even going beyond the claims made by Willard in his public appearances, and these exaggerations came to the attention of FDA. The agency, in just a few months, found Willard's Water being promoted as a treatment for arthritis, acne, anxiety, nervous stomach, high blood pressure, ulcers, digestive problems, colds, strep throat infections, psoriasis, burns, sore muscles and stress. According to the claims, it was useful for growing hair and preserving foods, for the care of goldfish and for houseplant ailments, for improved cooking and facial beauty, for doing the laundry, and for treating cancer in cows and leukemia in cats.

It is the medical claims that concern FDA. Products that are sold for such uses are considered drugs under the law. Before they can be marketed, the manufacturer must show that they



WILLARD'S WATER

As Seen On CBS "60 Minutes"

Has Been Tested On Plants, Heals Burns,
Psoriasis, Acne, Colds, Strep Throat,
Reduces Anxiety, Nervous Stomachs,
Cleans, Shampoos, Bathes, Enhances
Cooking, and More.

$13.50 Per Bottle
Postage Paid

Mail To:
SOLVENT, INC.
P.O. Box 12510
K.C., KS.
299-9511
or

FINE ARTS & SOLVENT STORE
6000 Leavenworth Rd.
K.C., KS.
299-6827

HOURS: MON-SAT. 9:30-5:30

DONALD R. HENDRICKSON, PRES.
EXCLUSIVE K.C. DISTRIBUTOR

are safe and effective for the uses intended. There is no such evidence available for Willard's Water, by the firm's own admission.

The success of Willard's Water has brought other firms into the market with their own versions of catalyst altered water. One is Donino Chemical Co. of New York, which has met with FDA officials to discuss marketing requirements of its "Biowater" as a cosmetic, food additive, or human and veterinary drug. However, Donino has not yet filed any data or made applications to FDA for this.

Both FDA and other laboratories have analyzed the Willard's Water products and found that they contain various combinations of rock salt, lignite, sodium metasilicate, sulfated castor oil, calcium chloride and magnesium sulfate. No tannic or humic acid, substances that may cause liver damage, have been found in Willard's Water or similar products as some competitors have claimed. And FDA has not received reports of adverse reactions from catalyst altered waters.

The medical benefits claimed for Willard's Water and similar products are illegal under the Food, Drug, and Cosmetic Act. The statement by William J. Willard disavowing medical claims for the water came after the law's provisions were pointed out. Willard also included the following in his statement:

- When notified by FDA that a CAW Industries distributor is making such new drug claims, the firm will take action to stop them.
- Dr. John Wesley Willard, no longer a company officer or employee, will make no claims in his public appearances that CAW Industries' products are effective in the cure, treatment, mitigation or prevention of any disease in man or animals.

Richard C. Thompson is a member of FDA's public affairs staff.

Unwelcome Pesticide

When the ground is frozen and snowbanks are high, Americans still want fresh produce. To satisfy this demand, foreign exporters ship millions of pounds of fresh fruit and vegetables into the United States each year. It is the job of FDA's field personnel to assure that imported produce is safe and wholesome and free of such contaminants as insects, mold and illegal pesticide residues.

Last winter FDA's **Orlando district** office collected routine samples of fresh snow peas offered for import from Guatemala. Analysis by the Atlanta regional laboratory revealed a problem: Some of the samples contained residues of the pesticide chlorothalonil. Pesticide residues are allowable only when the Environmental Protection Agency sets a tolerance, or acceptable level of residue. Otherwise, the fruits or vegetables containing the residues are in violation of the Food, Drug, and Cosmetic Act. There is no EPA tolerance for chlorothalonil in snow peas.

Orlando investigators took additional samples from eight shippers offering snow peas from Guatemala, and analysis revealed the residue problem in seven. The district recommended that FDA automatically detain all lots of snow peas from Guatemala. Headquarters approval resulted in an automatic detention and an import alert to every field office warning about the problem.

Under automatic detention, all lots of the product offered for import from the specified sources are rejected unless the shipper can prove that the product does not violate the law. This step may be taken when examination of shipments from a particular source shows such a repeated or flagrant history of violations that a strong possibility exists that any given shipment from that source will be in violation.

In this case, FDA required each entry of snow peas to be supported by a certificate of analysis indicating that the product contained no residue of chlorothalonil. Guatemalan laboratories provided the certificates of analysis, and spot checks of certified shipments were also made by the Atlanta laboratory.

Since samples from one of the eight shippers had revealed no pesticide residues, the firm was granted an exemption from the certification requirements. Six of the seven remaining firms provided written responses indicating that use of the pesticide had been discontinued. The automatic detention was lifted from each firm as FDA analysis confirmed that their shipments were consistently free of chlorothalonil.

Home Sweet Home?

Mice aren't too demanding about what they eat or where they live, mate, bear young or die.

During an inspection of a warehouse in Tullahoma, Tenn., an FDA **Nashville district** investigator found a nest occupied by five baby mice and five adults in a case of jellybeans. Another nest with 10 baby mice was in

a bag of
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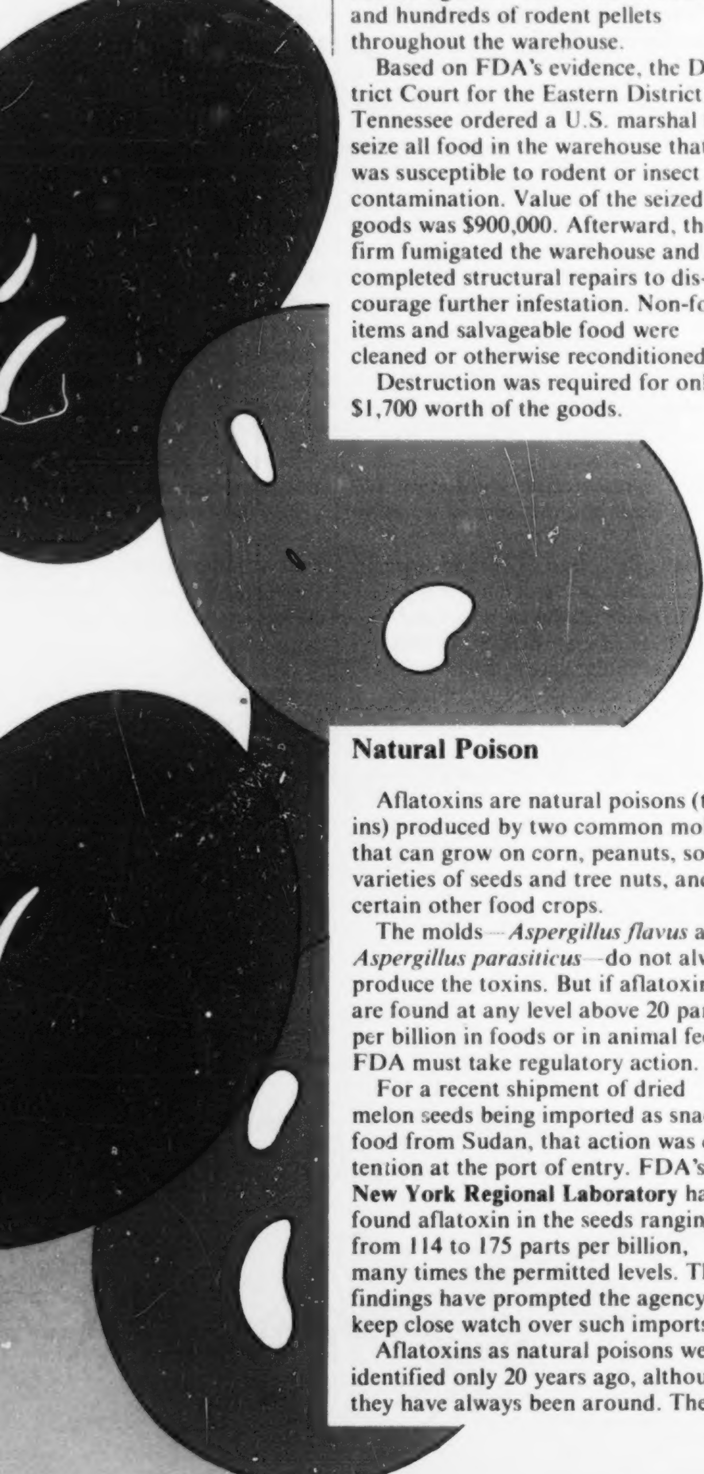
mix.

dogfood. Nearby, three mice
bling at table salt. There were
mice, as well as gnawing
xcreta and urine stains to
ey'd been living in or on at
lots of food. There were also
cts in rice, oatmeal and flour

The warehouse owner, Smith and Son Wholesale Co. Inc., asked for 30 to 60 days to correct the trouble before FDA reinspected. But there was not much change five weeks later when the investigator returned and saw four live and nine dead mice, rodent signs in over 70 lots of food, and hundreds of rodent pellets throughout the warehouse.

Based on FDA's evidence, the District Court for the Eastern District of Tennessee ordered a U.S. marshal to seize all food in the warehouse that was susceptible to rodent or insect contamination. Value of the seized goods was $900,000. Afterward, the firm fumigated the warehouse and completed structural repairs to discourage further infestation. Non-food items and salvageable food were cleaned or otherwise reconditioned.

Destruction was required for only $1,700 worth of the goods.



Natural Poison

Aflatoxins are natural poisons (toxins) produced by two common molds that can grow on corn, peanuts, some varieties of seeds and tree nuts, and certain other food crops.

The molds—*Aspergillus flavus* and *Aspergillus parasiticus*—do not always produce the toxins. But if aflatoxins are found at any level above 20 parts per billion in foods or in animal feed, FDA must take regulatory action.

For a recent shipment of dried melon seeds being imported as snack food from Sudan, that action was detention at the port of entry. FDA's **New York Regional Laboratory** had found aflatoxin in the seeds ranging from 114 to 175 parts per billion, many times the permitted levels. These findings have prompted the agency to keep close watch over such imports.

Aflatoxins as natural poisons were identified only 20 years ago, although they have always been around. They are much more toxic than some man-made chemicals and are known to cause cancer, liver damage and other illnesses.

At first it was thought that the molds would grow and the toxins be formed only when the peanuts, corn and other crops were stored under faulty conditions. Now it has been discovered that crops are susceptible to the mold while still in the field, even before harvesting. This has been a problem to farmers in recent years, especially those who grow corn in the Southeastern states, caught in cycles of drought, insect damage and other conditions that encourage growth of the mold. (See "Aflatoxins: Hazards From Nature," *FDA Consumer*, May 1978.)

Quarantine

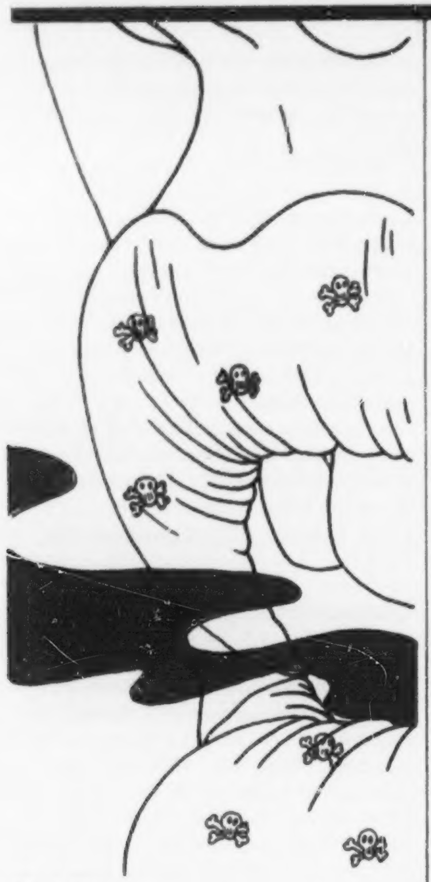
An investigator from FDA's **Newark district** office was looking at the stocks and records of Pharmadyne Laboratories, a drug manufacturer in Elmwood Park, N.J., that had just gone out of business. He noted that Pharmadyne had made shipments to Bioline Labs, a distributor in Brooklyn, and that information on some of the shipments, including a recalled product, seemed incomplete. He asked the **New York district** to check this.

Visiting Bioline, the New York inspector found four lots of tablets labeled dihydroergotoxine mesylate, a drug for treatment of senility, that Bioline had received from Pharmadyne. At the time, Bioline had doubts about the tablets and had them analyzed by a private laboratory.

The tests showed the tablets were placebos with no active ingredients and were not at all the drug they were claimed to be. Bioline then recalled the tablets it had distributed, for return to the manufacturer.

But there was no longer a manufacturer, since Pharmadyne had gone out of business. With no place to send the mislabeled drugs, Bioline placed them in a quarantine area under lock and key, which is where the FDA investigator found them.

The agency's New York Regional Laboratory tested the tablets and confirmed that they were placebos, not a senility drug. With that confirmation, Bioline destroyed the entire four lots, valued at $58,700.



Hot Pop

One sip apiece, and two Dayton, Ohio, residents wound up in an emergency room last April for treatment of caustic burns of the mouth and throat.

Both individuals became ill after drinking Mountain Dew, a soft drink in 16-ounce bottles, which contained a 3.8 percent solution of sodium hydroxide, a potent bottle-washing detergent used in the soft drink industry to sterilize bottles.

FDA's **Cincinnati district** office was notified by the Montgomery County (Ohio) Health Department. Samples from the contents of the two bottles were analyzed by FDA's Cincinnati laboratory and the caustic fluid discovered.

Pepsi-Cola Bottlers manufactures the citrus-flavored, carbonated soft drink. The Dayton franchise, owned by GCC Beverages Inc., recalled about 866,000 of the 16-ounce bottles of Mountain Dew that had been distributed in eight west-central Ohio counties.

The cause of the problem was not definitely determined.

FDA Upheld on Shrimp

The headless, deveined and frozen shrimp had traveled halfway around the world to reach the Port of New York, but the shipment, which originated in India, was doomed from the start.

When the shrimp arrived in New York in April 1979, FDA investigators from the **New York district** office in Brooklyn found evidence of *Salmonella* contamination in all three lots offered for import. *Salmonella* bacteria in the digestive tract cause salmonellosis, a contagious disease characterized by diarrhea, fever and kidney problems. The *Salmonella* in the shrimp resulted from improper handling and insanitary processing in India. FDA refused to permit importation of the shrimp to this country, saying the product was adulterated. A hearing was held and after reviewing the evidence, FDA issued a "Notice of Refusal of Admission."

FDA representatives and Indian trade officials had met several times in February 1979 in efforts to forestall automatic detention of shrimp from India. An automatic detention is an administrative action by which the agency detains a particular product from a particular source without laboratory analysis because of a history of violations involving the product and source.

A month after the three lots of contaminated shrimp arrived at the Port of New York, an FDA delegation was invited to India to inspect shrimp processing plants. Numerous insanitary conditions were observed, any one of which could have contributed to the shrimp contamination.

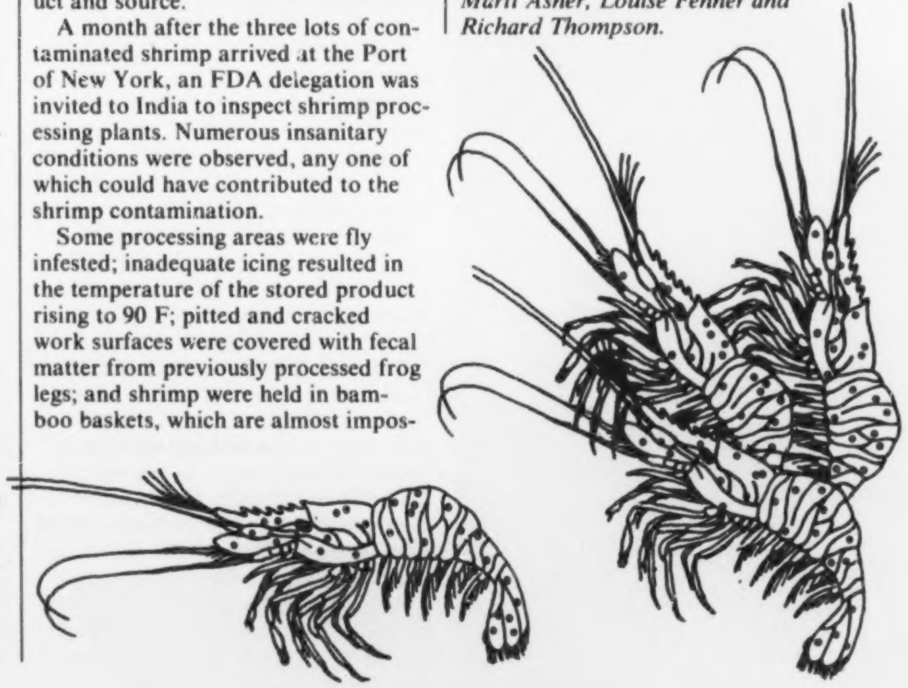
Some processing areas were fly infested; inadequate icing resulted in the temperature of the stored product rising to 90 F; pitted and cracked work surfaces were covered with fecal matter from previously processed frog legs; and shrimp were held in bamboo baskets, which are almost impossible to sterilize.

When the FDA delegation returned to the United States, the agency imposed automatic detention on all shrimp from India. This action was taken based on the observations of the delegation, as well as on a large number of import shipments from India over the previous several months that had been found contaminated with *Salmonella*. The three lots detained in New York were re-exported to other countries.

Continental Seafoods Inc., importers of the shrimp, filed suit in the U.S. District Court, which sustained FDA's decision. In March 1982 the U.S. Court of Appeals for the District of Columbia upheld FDA's decision.

Since then, "It appears that the Indians have made great strides in improving overall shrimp processing conditions," reports Gary J. Dykstra, chief of the regulatory operations section of FDA's Office of Regulatory Affairs. The Indian government has instituted a certification program in which only those firms participating in the program can export to the United States. Negotiations continue between FDA and the Indian government in efforts to remove automatic detention requirements.

—This small sample of reports from the field was compiled and written by Marti Asner, Louise Fenner and Richard Thompson.



Seizures

FILED SEIZURE ACTIONS charge violations of the Federal Food, Drug, and Cosmetic Act and are initiated based upon FDA recommendations. A seizure action is commenced by the filing in the U.S. district court where the goods are located. A U.S. marshal is then directed by the court to take possession of the goods, removing the product from commerce, until the matter is resolved.

A total of 12 actions to remove from the consumer market products charged to be violative was reported in May and June. These actions included 10 of foods: 1 involved charges concerning poisonous and deleterious substances, 7 involved charges concerning contamination, spoilage or insanitary handling, 1 involved economic and labeling violations, and 1 involved food additives. Others included 1 of cosmetics and 1 of medical devices.

PRODUCT, DISTRICT & DATE FILED	FIRM & PLACE OF BUSINESS	CHARGES
	FOOD/Poisonous and Deleterious Substances	
Fish fillets, frozen/U.S. District Court for the District of New Jersey 5/22/82	Imported from Panama.	Articles contain the deleterious substance histamine in such quantities as to ordinarily render them injurious to health; articles contain decomposed fish; the labeling of the articles falsely and misleadingly represents the articles as being red snapper.
	FOOD/Contamination, Spoilage, Insanitary Handling	
Flour, macaroni products, sugar, and other food stocks/U.S. District Court for the Northern District of New York 6/2/82	R. Pusatere Inc./Troy, N.Y.	Products were held under insanitary conditions, and certain of the articles contain rodent filth.
Macaroni products/U.S. District Court for the District of Puerto Rico 5/10/82	Freiria & Co. Inc./Puerto Nuevo, Puerto Rico	Products contain insects, and were held under insanitary conditions.
Mole, a seasoning paste/U.S. District Court for the District of Illinois 4/16/82	Imported from Mexico.	Product contains insect, bird, rodent and other filth; also, the label was not in the English language.
Pinto beans/U.S. District Court for the Eastern District of Washington 4/30/82	Northwest Produce Co. Inc./ Yakima, Wash.	Product was held under insanitary conditions.
Rice, Sello Rojo/U.S. District Court for the District of Puerto Rico 4/8/82	Rice Growers Association of California (Puerto Rico) Inc./Guaynabo, Puerto Rico	Product contains insect filth and was held under insanitary conditions.
Rice/U.S. District Court for the District of Puerto Rico 5/24/82	Farmers Rice Co. of Puerto Rico Inc./Guaynabo, Puerto Rico	Product contains insect and rodent filth and was held under insanitary conditions.
Sunflower seeds/U.S. District Court for the Eastern District of Missouri 4/19/82	Shipped from Fargo, N.D.	Product contains insect filth and was held under insanitary conditions.
	FOOD/Economic and Labeling Violations	
Syrup/U.S. District Court for the Southern District of Mississippi 5/7/82	Norris Brothers/West Monroe, La.	Corn syrup has been substituted in part for the company's "Sorghum Syrup, Cane Molasses & Sugar Syrup"; labeling false and misleading in that it represents that the food is a sorghum syrup, cane molasses, and cane sugar mixture, when the food contains corn syrup; the article fails to bear the name of the food and the name of each optional ingredient, as specified in the definition and standard of identity for table syrup.
	FOOD ADDITIVES	
Cake decorating wafers/U.S. District Court for the Northern District of Illinois 4/5/82	Imported from Italy and West Germany.	Product contains the non-conforming food color additives FD&C Red #2 and Cochineal Red A.
	COSMETICS	
Tablets of canthaxanthin and beta-carotene for all-over tan without the sun/U.S. District Court for the District of New Jersey 5/4/82	Cosmetest Corp./E. Rutherford, N.J.	Product contains the non-conforming color additives canthaxanthin and beta-carotene.
	MEDICAL DEVICES	
Bandages and bandage components/U.S. District Court for the Western District of New York 6/1/82	Medex Products Corp./Buffalo, N.Y.	Products were prepared, packed and held under insanitary conditions; the circumstances used for the products' manufacture, packing and storage are not in conformity with regulations.

Notices of Judgment

NOTICES OF JUDGMENT on Seizure Actions

FOOD/Contamination, Spoilage, Insanitary Handling

Beans, green, canned, at Sand Springs, N. Dist. Okla.
Charged 9-16-80: while held for sale, the article was held in swollen cans and contained decomposed green beans; 402(a)(3). Default decree ordered destruction. (F.D.C. No. 63168; S. No. 80-266-114; N.J. No. 1)

Grapefruit sections, canned, at St. Louis, E. Dist. Mo.
Charged 1-21-82: when shipped by Morris Canning Co., Winter Haven, Fla., the article had been held in cans which were too small and leaking; 402(a)(3). Default decree ordered destruction. (F.D.C. No. 63633; S. No. 82-257-597; N.J. No. 2)

Lupini beans, oregano leaves, and **flour,** at Chicago, N. Dist. Ill.
Charged 11-25-81: while held by Joseph Antognoli & Co., Chicago, Ill., the articles had been held under insanitary conditions; 402(a)(4). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63605; S. No. 82-177-368; N.J. No. 3)

Peanut butter candy cups, chocolate bars, caramel bars, crackers, gum, and **other confectionary stocks,** at Buffalo, W. Dist. N.Y.
Charged 4-1-82: while held by Shosho Brothers Inc., Buffalo, N.Y., the candy cups and caramel bars contained rodent filth, and all of the articles had been held under insanitary conditions; 402(a)(3), 402(a)(4). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63695; S. No. 82-285-572; N.J. No. 4)

Peanuts, shelled, at San Francisco, N. Dist. Calif.
Charged 3-15-82: while held by Art's Trading Co., San Francisco, Calif., the article contained rodent filth and had been held under insanitary conditions; 402(a)(3), 402(a)(4). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63679; S. No. 82-390-846; N.J. No. 5)

Pecan pieces, at Albany, M. Dist. Ga.
Charged 2-11-82: when shipped by Pippin Pecan Co. Inc., Albany, Ga., the article had been prepared, packed or held under insanitary conditions; 402(a)(4). Consent decree authorized release to the shipper for salvaging. (F.D.C. No. 63644; S. No. 82-260-321; N.J. No. 6)

Rice flour, at St. Louis, E. Dist. Mo.
Charged 1-12-82: while in transit and when shipped from Memphis, Tenn., the article had been held under insanitary conditions; 402(a)(4). Default decree ordered destruction. (F.D.C. No. 63615; S. No. 82-256-959; N.J. No. 7)

Sauces, chili and bean, at Chicago, N. Dist. Ill.
Charged 11-25-81: while held for sale, the articles contained mold and were contained in leaking jars; 402(a)(3). Default decree ordered destruction. (F.D.C. No. 63600; S. No. 81-291-926 et al.; N.J. No. 8)

Sugar, and **other food stocks,** at Tullahoma, E. Dist. Tenn.
Charged 3-2-82: while held by Smith & Son Wholesale Co. Inc., Tullahoma, Tenn., the articles had been held under insanitary conditions; 402(a)(4). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63660; S. No. 82-276-329; N.J. No. 9)

Walnuts, pecans, brazil nuts, and **mixed nuts (all unshelled),** at Oklahoma City, W. Dist. Okla.
Charged 11-19-81: while held by Frank's Tomato and Banana House, (Tanaka Produce Inc.), Oklahoma City, Okla., the articles had been held under insanitary conditions; 402(a)(3). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63586; S. No. 81-209-898; N.J. No. 10)

Whiting fish, headless, frozen, at Columbus, M. Dist. Ga.
Charged 12-22-81: when shipped from Massachusetts, the article, labeled in part (case) "H&G Whiting . . . Boothbay Fisheries, Inc., Boston, Mass" and (box) "Eastern seas . . . Quick Frozen Fillets Product of Canada . . . Headless Whiting . . . Distributed By . . . Eastern Point Seafoods, Inc. . . . Glouchester, Ma.," contained decomposed headless whiting fish; and the article's label contained the false and misleading label statement "fillets"; 402(a)(3), 403(a)(1) Default decree ordered destruction. (F.D.C. No. 63604; S. No. 82-289-419; N.J. No. 11)

FOOD/Economic and Labeling Violations

"Concentrated orange juice for manufacturing," at San Jose, N. Dist. Calif.
Charged 2-24-82: when shipped by Fresh Pak Foods Inc., McAllen, Texas, the color turmeric had been added to make the article appear better or of greater value than it was—402(b)(4); the article contained the non-conforming color additive turmeric—402(c); the article's name "Concentrated Orange Juice for Manufacturing" on the label was false and misleading because the article was not concentrated orange juice for manufacturing, since it contained the artificial color turmeric—403(a)(1); the article failed to conform to the definition and standard of identity for concentrated orange juice for manufacturing because it contained the added color turmeric—403(g)(1); and the article contained an artificial color (turmeric) and the label failed to reveal that fact—403(k). Default decree authorized donation to a charitable organization. (F.D.C. No. 63641; S. No. 82-345-781; N.J. No. 12)

"Orange juice from concentrate," at San Jose, N. Dist. Calif.
Charged 3-5-82: while held by Beech-Nut California Corp., San Jose, Calif., who had manufactured the article using "concentrated orange juice for manufacturing" shipped by Fresh Pak Foods Inc., McAllen, Texas (see N.J. No. 12 of this issue), the article contained the color turmeric so as to make it appear better or of greater value—402(b)(4); the article contained the non-conforming color additive turmeric—402(c); the article's name "Orange Juice From Concentrate" on the label was false and misleading, since the article did not meet the definition and standard of identity for orange juice from concentrate because it contained turmeric—403(a)(1); the article failed to conform to the definition and standard of identity for orange juice from concentrate since it contained the added color turmeric—403(g)(1); and the article contained the artificial color turmeric and the label failed to reveal that fact—403(k). Default decree ordered destruction. (F.D.C. No. 63664; S. No. 82-345-790; N.J. No. 13)

"Sole" fillets, at St. Louis, E. Dist. Mo.
Charged 10-31-78: when shipped by New York Sea Food Exchange, New York, N.Y., the article, labeled in part "IQF Sole Fillet Product of Holland," had had Greenland turbot substituted for sole—402(b)(2); the article's label was false and misleading in representing that the only fish in the article was sole—403(a)(1); Greenland turbot was offered for sale under the name of another food, "sole"—403(b); and the labels of the article lacked the common or usual name of the food because "sole" was not the common or usual name for Greenland turbot—403(i)(1). Consent decree authorized release to the shipper for relabeling. (F.D.C. No. 61941; S. No. 78-123-749; N.J. No. 14)

DRUGS/Human Use

Betamethasone valerate cream, at City of Industry, C. Dist. Calif.
Charged 3-6-81: when shipped by Premo Pharmaceutical Laboratories Inc., South Hackensack, N.J., the article was a new drug without

an effective approved New Drug Application—503(a); and its labeling lacked adequate directions for use and was not exempted due to its new drug status—502(f)(1). Default decree ordered destruction. (F.D.C. No. 63383; S. No. 81-258-705; N.J. No. 15)

Chlorothiazide tablets, two seizure actions, at Hollywood and Fort Lauderdale, S. Dist. Fla.
Charged 6-5-80 and 6-5-80: when shipped by Camall Co., Detroit, Mich., the article, labeled in part "Chlorothiazide . . . Manufactured . . . by Camall Co., Detroit," was a new drug without an effective approved New Drug Application; 505(a). Default decrees ordered destruction. (F.D.C. Nos. 62891, 62923; S. Nos. 80-197-875 & 80-193-660; N.J. No. 16)

Chlorthalidone tablets, at Hollywood, S. Dist. Fla.
Charged 12-11-80: when shipped by Zenith Laboratories Inc., Northvale, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (F.D.C. No. 63217; S. No. 80-239-255; N.J. No. 17)

Chlorthalidone with reserpine tablets, at City of Industry, C. Dist. Calif.
Charged 3-6-81: when shipped by Premo Pharmaceutical Laboratories Inc., South Hackensack, N.J., the article was a new drug without an effective approved New Drug Application—505(a); and the article's labeling lacked adequate directions for use and was not exempted due to its new drug status—502(f)(1). Default decree ordered destruction. (F.D.C. No. 63381; S. No. 81-258-705; N.J. No. 18)

Cough syrup, and **other drug stocks,** at Cleveland, N. Dist. Ohio.
Charged 7-30-79: when shipped by C. M. Bundy Co., Erlanger, Ky., the circumstances used for the articles' manufacture, processing, packing or holding failed to conform with current good manufacturing practice; 501(a)(2)(B). The article was claimed by Reese Chemical Co., Cleveland, Ohio. A consent decree authorized release to the claimant for salvaging. Subsequently, salvaging not being financially feasible, the parties jointly moved that the articles be destroyed, and the court ordered the articles destroyed. (F.D.C. No. 62327; S. No. 79-114-023; N.J. No. 19)

Diethylpropion HCl tablets, at San Mateo, N. Dist. Calif.
Charged 8-6-81: when shipped by Premo Pharmaceutical Laboratories Inc., South Hackensack, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (F.D.C. No. 63522; S. No. 81-247-776; N.J. No. 20)

Renacidin 10% solution, at Milwaukee, E. Dist. Wis.
Charged 3-3-81: when shipped by K-N Enterprises Inc., t/a Iota Corp., Skokie, Ill., the article was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (F.D.C. No. 63334; S. No. 81-201-713; N.J. No. 21)

Triamterene-hydrochlorothiazide capsules, doxylamine succinate with pyridoxine HCl tablets, hydroxyzine HCl tablets, Hydergot sublingual tablets, hydroxyzine pamoate capsules, betamethasone valerate cream, allopurinol tablets, trifluoperazine HCl tablets, and **chlorthalidone tablets,** at New Britain, Dist. Conn.
Charged 5-12-80: when shipped by Premo Pharmaceutical Laboratories Inc., South Hackensack, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The articles were claimed by the shipper who denied the charge. Subsequently, the action was transferred to the district of New Jersey. Ultimately, upon joint motion of the parties, the articles were ordered destroyed. (F.D.C. No. 62863; S. Nos. 80-191-134/5; N.J. No. 22)

DRUGS/Veterinary

Expectorant for horses and dogs, at Cleveland, N. Dist. Ohio.
Charged 7-30-79: when shipped by C. M. Bundy Co., Erlanger, Ky., the circumstances used for the manufacture, processing, packing or holding of the article failed to conform with current good manufacturing practice; 501(a)(2)(B). Consent decree authorized release to Williams Drug Distributors Inc., Cleveland, Ohio, for salvaging. Subsequently, it became apparent that salvaging of the article was not financially feasible. Upon joint motion of the parties to destroy the article and cancel and discharge the claimant's bond, the court ordered the article destroyed, ordered payment by the claimant of the costs of destruction, and, upon such payment, ordered the claimant's bond discharged. (F.D.C. No. 62328; S. No. 79-114-027 et al.; N.J. No. 23)

Oxytetracycline HCl preparations for veterinary uses, at Kansas City, W. Dist. Mo.
Charged 4-25-77: while held by I. D. Russell Co. Laboratory, Kansas City, Mo., who had manufactured the articles using interstate oxytetracycline HCl, the articles were new animal drugs and no approvals of New Animal Drug Applications were in effect with respect to their use and intended uses—501(a)(5); and certain preparations (coded "51093," "51094" and "12353") differed from their purported strength because the articles contained less oxytetracycline hydrochloride than was declared on their labels—501(c).

The articles were claimed by the manufacturer who denied the charges. The parties served written interrogatories on each other. After discovery in the action had been closed, the government moved to compel the defendant to comply with the district's standard pretrial order for filing lists of witnesses and exhibits. The court granted the government's motion. The claimant filed the required lists of witnesses and exhibits and also moved for an order granting permission to take a deposition.

Subsequently, the court issued a show cause order against the claimant concerning failure to comply with a deadline. The claimant responded that the delay was unintentional and inadvertent and requested permission to file its response forthwith. The government subsequently moved to amend its witness list to include two additional experts. The court granted the motion. Meanwhile, the articles were substantially damaged and destroyed by a fire at the manufacturer's plant.

Pursuant to stipulation, the parties jointly moved to dismiss the action, without prejudice, as *moot* on the following grounds: the oxytetracycline HCl product "RV-VI-OXY" was no longer in production or distribution, and the manufacturer would not produce or distribute "RV-VI-OXY" without the prior written permission and approval of FDA; and the articles recited in the complaint had been destroyed by a fire, so the *res* no longer existed. The court ordered the action dismissed without prejudice and ordered that each side bear its own costs. (F.D.C. No. 61173; S. No. 77-24-342 et al.; N.J. No. 24)

"Skin Medicine" for horses and dogs, at Jupiter, S. Dist. Fla.
Charged 7-25-80: while held by Jupiter Veterinary Products, Jupiter, Fla., who manufactured the article using interstate camphor, the article was a new animal drug and no approval of a New Animal Drug Application was in effect with respect to its use or intended use—501(a)(5); and the article had been manufactured, prepared, compounded and processed in an unregistered establishment—502(o). Default decree ordered destruction. (F.D.C. No. 63117; S. No. 80-166-721; N.J. No. 25)

Various drug stocks for veterinary use and various syringes and other

devices for veterinary use, at Peoria, C. Dist. Ill.

Charged 9-30-80: while held by Miller Chemical Co., Peoria, Ill., the circumstances used for the holding of the drugs failed to conform with current good manufacturing practice, and the facilities and controls used for the storage of the devices failed to conform with prescribed regulations, since both the drugs and devices had been exposed to exploding chemicals, intense heat, smoke, soot and water damage as a result of a fire at the dealer's distribution center; 501(a)(2)(B), 501(h). Default decree ordered destruction. (F.D.C. No. 63156; S. No. 80-248-245; N.J. No. 26)

MEDICAL DEVICES

Adhesive patch with magnet, Acu-Dot, at Fort Lauderdale, S. Dist. Fla.

Charged 1-18-80: the article, which had been distributed by Acu-Dot International Pharmaceutical Co. Ltd., Akron, Ohio, and which was labeled in part "Acu-Dot Magnetic Analgesic Patch . . . Mfg. For temporary relief of occasional minor aches and pains of muscles and joints Mfg. for Acu-Dot International Pharmaceutical Co., Ltd. . . . Akron, Ohio," had false and misleading labeling since the article had not been shown to be adequate or effective for such intended use—502(a); the article's labeling lacked adequate directions for its intended purposes—502(f)(1). Default decree ordered destruction. (F.D.C. No. 62711; S. No. 80-193-640; N.J. No. 27)

Slendertone muscle stimulators, at Great Neck, E. Dist. N.Y.

Charged 2-13-81: the article, which was held by Passive Fitness Inc., Great Neck, N.Y., was accompanied by promotional materials (newspaper and magazine article reprints) which contained false and misleading claims for the article concerning losing inches and flab without physical exercise, revitalizing muscles without physical exercise, and breaking down toxic wastes and deposits trapped between layers of connective tissue with resulting loss of weight and inches—502(a); the article's labeling lacked adequate directions for lay use, since the article was ineffective for its promoted uses, was potentially harmful and was offered for use without a prescription—502(f)(1); the article's labeling lacked adequate warnings against unsafe use (e.g., use in pregnant women and individuals with cardiac conditions or vascular disorders)—502(f)(2). Default decree ordered destruction. (F.D.C. No. 63096; S. No. 80-194-208; N.J. No. 28)

X-ray system, Traceray III, at Redford, E. Dist. Mich.

Charged 10-5-79: the article, which had been manufactured by Western States Supply Ltd., Pueblo, Colo., was dangerous to health when used as directed because the article would emit radiation beyond the pre-set exposure time—502(j); the accompanying labeling was false and misleading in claiming compliance with the regulation's standards, and in claiming that the devices would deliver the radiation exposure stated in the instruction manual—502(a); and the article's quality fell below its purported quality—501(c). Default decree ordered destruction. Consent decree authorized release to the possessor for reconditioning. (F.D.C. No. 62505; S. No. 79-120-714; N.J. No. 29)

NOTICES OF JUDGMENT on Criminal Actions

Morton-Norwich Products Inc., t/a Norwich Pharmacal Co., and James J. Mahoney, operations vice president, Norwich, N. Dist. N.Y.

Charged 9-30-75 by grand jury: when Furacin nitrofurazone-impregnated gauze pads (counts 1-3) were shipped, the circumstances used for the article's manufacture, processing, packing and holding failed to conform with current good manufacturing practice, and the purity of the article differed from its purported purity (i.e., "sterile"), since the article was contaminated with mold; 501(a)(2)(B), 501(c). The defendants pleaded not guilty. The defendants requested that the government produce for inspection and copying a number of specified documents. (See N.J. No. 33 of this issue of *FDA Consumer.*)

The court denied a motion by the defendants to dismiss the "current" good manufacturing practice charges, saying:

"The defendants, above-named, have moved to dismiss a portion of each of the three counts in the above numbered indictment each of which charges them with a violation of 21 U.S.C. §351(a)(2)(B) on the grounds that they are being denied their Fifth and Sixth Amendment rights, (1) because Section 351(a)(2)(B) is unconstitutionally vague as enacted, (2) because the regulations promulgated in connection with Section 351(a)(2)(B) are unconstitutionally vague, (3) because the application to the defendants of Section 351(a)(2)(B) and of the regulations is unconstitutional, and (4) because the indictment, which in the part challenged, only tracks the language of the statute and is unconstitutionally vague.

"Defendant, Morton-Norwich Products, Inc. (Norwich), is a pharmaceutical company which manufactures, among other things, a sterile gauze pad impregnated with Furacin. These dressings are applied to wounds, burns, etc. The gauze pad is automatically enclosed and sealed in a paper foil container under sterile conditions. The packages thus prepared are 100 percent inspected before packing to assure the integrity of the package and therefore presumably the continued sterile condition of the medicated pad. Defendant, James J. Mahoney (Mahoney), is the operations vice president of Norwich.

"The first paragraph of each of the counts in this indictment which was filed on Sept. 30, 1975, recites that between particular dates or on certain dates Norwich introduced into interstate commerce certain shipments of Furacin gauze pads with specific destinations. The first charge in each count which defendants find objectionable provides: 'That said drug, when caused to be introduced and delivered for introduction into interstate commerce, as aforesaid was adulterated within the meaning of 21 U.S.C. 351(a)(2)(B) in that the methods used for the manufacture, processing, packing and holding of said drug did not conform to and were not operated and administered in conformity with current good manufacturing practice to assure that said drug would meet the requirements of the Federal Food, Drug, and Cosmetic Act as to safety and would have the identity and strength and would meet the quality and purity characteristics which it purported and was represented to possess.'

"No definition of 'current good manufacturing practice' (CGMP) is contained in either the statute or the rules and regulations issued under it.

"It is clear from reading the affidavits of the experts employed by both parties that the term current good manufacturing practice is and of necessity must be flexible in its application to the manufacture of particular drugs. Furthermore, considering the end to be accomplished, i.e., the identity, strength, quality and purity of the drugs being introduced into commerce for the purpose of use by human beings, improvements and consequent change in what is CGMP is always to be anticipated as well as a desired end. The ultimate test of CGMP therefore is whether it results in a product which possesses the characteristics which the manufacturer represents it to have and whether the methods used to produce it are designed to assure that result.

"A review of the legislative history of this section as contained in the affidavits and memoranda supplied and an examination of the cases which have been cited which have upheld the constitutionality of the statute leads me to the conclusion that there is not only a sufficient standard but also that the statute is not void for vagueness.

"The considerations inevitably leading to this conclusion are that the manufacturers participated in the legislative hearings which resulted in the legislation and regulations, that there are many publications which discuss CGMP, college courses dealing with the subject, Food and Drug Administration (FDA) seminars and courses and various trade associations which concern themselves with this subject as well as other matters coming under the jurisdiction of the FDA.

"It is undoubtedly true that the manufacturer of drugs must assume hazards which may be different from those which others bear but that is not unfair.

"Similarly, and for the reasons stated I do not find the regulations promulgated under 21 U.S.C. §351(a)(2)(B) void for vagueness nor do I find their application to these defendants unconstitutional either for vagueness or because they fail to satisfy due process requirements.

"An examination of the regulations provide a sufficient standard with respect to basic essentials as evidenced by Part 133 'Drugs: Current Good Manufacturing Practice in Manufacture, Processing, Packing or Holding.' The fact that proposed new regulations have been prepared to supersede those in effect in 1973 and that FDA has recognized the need for more specificity does not affect the validity of the regulations applicable here. I see no reason why this claim for more specificity does not fall within the ambit of those cases which have held that although a statute might have been drawn more precisely does not make it unconstitutional. . . .

"I adopt the language of the Court in *United States* v. *Bel-Mar Laboratories, Inc.*, 284 F. Supp. 875, 883 (E.D.N.Y. 1968) which explicitly approved the CGMP regulations. . . .

"Finally it should be noted that we are dealing here with an established manufacturer. It is incredible that they now claim that they do not know what CGMP is in view of the in-house memoranda to make sure that they were in compliance with CGMP and their certification to FDA when approval of the Furacin products were sought that the product was to be manufactured in accordance with current good manufacturing practice.

"It is the rule in this Circuit that an indictment which tracks the language of the statute is sufficient to withstand an attack based upon the requirements of the Fifth and Sixth Amendments and Rule 7(c)(1) of the *Federal Rules of Criminal Procedure*. The language is sufficient if it tracks the language of the statute and provides enough information to assure against double jeopardy. . . .

"I do not find the requisite prejudice demonstrated here. The defendants obviously have recourse to a bill of particulars and discovery to ascertain in what areas the government will prove beyond a reasonable doubt their operation was not in compliance with CGMP.

"The motion with respect to each count is denied."

After additional litigation, the defendants waived jury trial and, with the government's consent, the case was tried by the court. Trial commenced on Jan. 13, 1977, and this case was taken under submission on March 18, 1977. On Aug. 18, 1978, the court returned a general verdict finding the individual not guilty on all counts, finding the corporation not guilty on Count 3, not guilty of the current good manufacturing practice charges, and finding the corporation guilty on Counts 1 & 2. Following the verdict, the corporation moved to have the verdict set aside and moved for acquittal on the following grounds: (1) that the government's post-shipment testing of pads (in which mold was detected) was prejudicial and irrelevant in view of the defendant's testing prior to shipment; (2) that the government was estopped due to reliance by the defendant on an FDA assurance in 1973 that its test methods were adequate; (3) that the court erred in not striking the testimony of Dr. Philip Mislivic because the cultures upon which he based his testimony had been destroyed and his testimony had not been properly connected; (4) that the testimony of FDA inspector Donald Howard before the grand jury was so prejudicial that the grand jury had been unable to render a proper verdict; and (5) that the time delay between the submission of the case and the verdict violated the corporation's rights to due process and to a speedy trial.

The court denied the firm's motion, saying:

"This is a criminal action involving three alleged violations of the Federal Food, Drug, and Cosmetic Act, Title 21 U.S.C. §§301, et seq. Named as defendants in the Indictment are Morton-Norwich Products, Inc., a corporation doing business as Norwich Pharmacal Company, and James J. Mahoney, Vice-President of Operations for Morton-Norwich Products, Inc.

"Indictment Number 75-CR-114, which was handed up on or about Sept. 30, 1975, alleges three violations by both defendants of the Food, Drug, and Cosmetic Act, all of which violations involve the interstate shipment of adulterated drugs, in contravention of sections 301(a) and 303 of the Act, 21 U.S.C. §§331(a) and 333 respectively. Each count, in turn, alleges adulteration in two separate and distinct senses, one falling within section 501(c), 21 U.S.C. §351(c), in that the purity of the drugs involved differed from that purported, the other coming under section 501(a)(2)(B), 21 U.S.C. §351(a)(2)(B), contending that the drugs were not manufactured, processed, packaged or held in conformity with current good manufacturing practice so as to assure that they would conform to the Food, Drug, and Cosmetic Act requirements as to safety, and would have the strength and identity and meet the quality and purity characteristics which they purported to possess (the (a)(2)(B) violation will be referred to simply as CGMP).

"The products involved in the three counts of the Indictment are two lots, numbered 705553 (Counts I and II) and 710749 (Count III), of individually packaged gauze pads impregnated with Furacin (trade name for nitrofurazone), an antibacterial dressing. All of the products involved were manufactured at the defendants' sterile fill facility located in Norwich, New York.

"The gravamen of the charge of adulteration under 21 U.S.C. §351(c) is that the pads, purported to be sterile according to the labeling found on the foil envelopes in which the pads were to be marketed, were not, in fact, sterile. The charge under 21 U.S.C. §351(a)(2)(B) relates to several alleged violations of CGMPs, based heavily upon observations made during Food and Drug Administration (FDA) inspections of the defendants' sterile fill facility at Norwich, as well as the actual evidence of product contamination.

"This Court conducted a rather lengthy non-jury trial of this action, commencing on Jan. 13, 1977, and ending on March 18, 1977. Following the trial, the Court reserved decision on the verdict. Since none of the parties requested that the Court make special findings, the general verdict was announced to the parties in open court. See *Fed. R. Crim. P.* Rule 23(c). To recapitulate, the Court found defendant Morton-Norwich guilty on Counts I and II and not guilty on Count III, and acquitted defendant Mahoney on all three charges.

"Prior to, during, and after the trial, the parties made numerous motions, upon many of which the Court reserved decision. This supplemental Opinion is being rendered in order to deal with those motions, and to hopefully clarify the verdict somewhat for the benefit of the parties.

I. Motion To Strike Government's Test Results

"Throughout this proceeding, the defendants have attacked, on three grounds, the introduction into evidence of the results of tests performed by FDA analysts on post-shipment specimens of product taken from the two lots in issue. First, they claim that owing to the fact that a sterility test such as involved in this case is necessarily destructive of the product unit tested, and because sterility in a manufacturing situation cannot be guaranteed on an absolute basis, sterility is necessarily a probabilistic concept. The defendants have insisted that their representation of sterility was proper in this case as long as pre-shipment tests, validly conducted by them in accordance with the

methods prescribed by the United States Pharmacopoeia (U.S.P.), indicated sterility, despite the fact that later tests revealed the presence of contamination in one or more samples of previously untested product. Secondly, the defendants attack the relevance of post-shipment tests with respect to the issue of sterility at the time of shipment. Finally, the defendants have sought to impeach the results of the Government's tests, pointing to several deviations of the methods used from that prescribed by the U.S.P.

A. Defendants' Representation of Sterility

"In support of their position on this score, the defendants, through various expert witnesses, have proffered definitions of the term 'sterility' or 'sterile,' all of which reject the notion of sterility as being an absolute concept in favor of a definition dependent upon results of probabilistic testing performed upon random samples of the product in accordance with U.S.P. testing methods. Thus, the argument goes, an article is properly labeled as 'sterile' if it has passed pre-shipment sterility tests performed pursuant to the U.S.P. method, notwithstanding the fact that some untested product units are in fact contaminated.

"The Court rejects the notion that the term 'sterile,' as contained within the labeling which accompanies the defendants' product, is susceptible of such a narrow interpretation. This Court is of the opinion that the meaning to be ascribed to labeling which accompanies a product is, like beauty, properly in the eyes of the beholder, rather than the manufacturer. Cf. *United States* v. *Article . . . Consist. of 216 Carton. Bot.*, 409 F.2d 734 (2d Cir. 1969). A customer who utilizes defendants' Furacin gauze or batiste pads, whether he be a doctor, a nurse, or a layman, in this Court's estimation, will interpret the representation of sterility to mean the total lack of contamination of the product. To allow the defendants to avoid liability under the Act merely by testing samples of the product, which samples prove negative for contamination, would be to obliterate the standard of absolute liability imposed by the Food, Drug, and Cosmetic Act, see *United States* v. *Park*, 421 U.S. 658 (1975); *United States* v. *Dotterweich*, 320 U.S. 277 (1943), and subtly inject into the statute an element of scienter, or conscious awareness of guilt. The Court believes that the relevant inquiry under 21 U.S.C. §351(c) is whether or not the gauze and batiste pads contained in Lots 705553 and 710749 were, in fact, sterile when shipped, utilizing an absolute definition of sterility.

"The defendants' motion to exclude the Government's test results upon this basis is accordingly denied.

B. Relevance of Post-Shipment Testing

"The clear import of 21 U.S.C. §331(a) is that in order to prove a violation of that provision, adulteration *at the time the product entered, or was delivered for introduction into, interstate commerce* must be proven beyond a reasonable doubt. *Penobscot Poultry Co.* v. *United States*, 244 F.2d 94 (1st Cir. 1957). Adulteration, of course, may be demonstrated by any logical and convincing means. *United States* v. *Lesser*, 66 F.2d 612 (2d Cir. 1933); cf. *Fed. Rules of Ev.* Rules 402, 702. One manner of proving pre-shipment adulteration is by showing adulteration after receipt at some point in time subsequent to travel in interstate commerce, together with proof that the adulteration necessarily occurred prior to shipment, rather than some later time. *Pasadena Research Laboratories* v. *United States*, 169 F.2d 375 (9th Cir. 1948), cert. den. 335 U.S. 853 (1948).

"The Court believes that the Government has sufficiently demonstrated that the post-shipment tests performed upon samples of their product are highly probative with regard to the issue of pre-shipment sterility. The defendants' motion to exclude those test results upon this basis is therefore denied.

C. Reliability of FDA Tests

"The defendants have drawn into issue the reliability of the FDA analysts' test results, pointing to various deviations of the methodology utilized from that prescribed by the U.S.P.

"In proving adulteration under 21 U.S.C. §351(c), the Government is not limited to any particular manner of proof, and is especially not limited to use of tests conducted in accordance with the U.S.P. *Woodard Laboratories* v. *United States*, 198 F.2d 995 (9th Cir. 1952). This Court has had ample opportunity to hear testimony from FDA analysts who performed the various post-shipment tests upon the products in issue. The Court was similarly able to view those analysts' test worksheets and to listen to numerous expert witnesses' opinions with regard to the validity of those tests. As must be obvious from the verdict, the Court has concluded that the tests conducted upon samples from Lot 705553 were valid, especially with regard to demonstrating pre-shipment contamination, and that the Government has proven pre-shipment adulteration of that lot beyond a reasonable doubt.

"A separate but related motion was made by the defendants to exclude certain of the Government's sterility test results (Government Exhibits 63, 64, and 78), based upon the Government's failure to preserve and produce records relating to the preparation and sterilization, by autoclaving, of the culture media utilized in the testing. . . .

"The Court is of the opinion that this deficiency relates not to the admissibility *vel non* of those test results, but merely to the weight to be accorded to them. In light of the use by the FDA analysts of both positive and negative controls, all of which produced results indicative of satisfactory testing conditions, the Court determines that the results of the tests are accurate and relevant and therefore should not be excluded.

"The defendants have also challenged the testimony of Leonard Mastrandrea, the FDA laboratory supervisor for the Brooklyn facility, as a portion of their attack upon the Government's test results. In particular, they contend that Mr. Mastrandrea's testimony as to lack of positive results in open controls on tests in which fleakers were used was hearsay, and should therefore be striken (T. 3261-3264). The Court is of the opinion that, with proof that all instances of positive results in those open controls would be reported to Mr. Mastrandrea, evidence of the absence of such reports is not hearsay, is highly relevant, and should therefore be admitted. See *McCormick on Evidence* §250 (2d Ed. 1972).

II. Motion To Strike Testimony Relating to Speciation of the Mold

"The defendants have moved to exclude testimony of Dr. Mislivic, an FDA mycologist who testified on behalf of the Government concerning his speciation of the molds cultured by the several FDA analysts during their testing of samples from defendants' Lot 705553 (T. 2412-2417; 2495; 3424). The defendants have also moved to strike testimony of Government expert witnesses, which testimony was based in part upon the speciations performed by Dr. Mislivic. The basis of their objection in this regard is Dr. Mislivic's failure to preserve the specimens from which he identified the presence of the mold *paecilomyces valioti*, which they claim effectively deprived them of their right to confront and cross-examine Dr. Mislivic, one of the Government's crucial witnesses.

"While the Court believes that the better practice would have been for Dr. Mislivic to preserve, in some manner, the samples actually speciated, whether by photograph or by maintaining the sample itself, especially since litigation was, at that point, virtually inevitable, the Court does not believe that his failure to do so rendered the results of those speciations inadmissible. Rather, it should merely affect the weight to be accorded to the results of his speciations. The defendants' motion in this regard is accordingly denied.

III. Motion To Dismiss Based Upon Allegedly False Grand Jury

Testimony

"The allegations set forth by the defendants in support of their motion to dismiss, based upon the prosecution's purported knowing use of perjured testimony before the Grand Jury in order to secure the instant Indictment, center around the testimony of Donald Howard. Mr. Howard was the FDA inspector whose observations during an inspection of defendant's Norwich sterile fill facility during June of 1973 form the core of the FDA's case concerning CGMP violations (T. 1935-1938; 1966-1987; 1990-2022; 3423). During his testimony before the Grand Jury, Mr. Howard characterized defendants' Norwich sterile fill facility as being in substantial violation of the CGMPs in June of 1973. He failed to mention to the Grand Jury, however, that he had inspected that same facility in February of 1973, and reported no major CGMP violations at that time. In fact, his testimony was such that the Grand Jury could reasonably have believed that the June inspection was Howard's first visit to the defendants' Norwich plant.

"This Court is indeed somewhat troubled with this aspect of Mr. Howard's testimony before the Grand Jury. That witness's characterizations of the Norwich facility as being in substantial violation of CGMPs are somewhat misleading when taken in context with the fact of his previous visit during which he failed to report any substantial violations.

"This Court has read the Grand Jury minutes of this case *in camera*, however, and is convinced that the Indictment is not vitiated by Mr. Howard's testimony. As should be obvious by now, the Court's verdict in this case with respect to Counts I and II was primarily the result of a finding of adulteration as defined in 21 U.S.C. §351(c), rather than any CGMP violation under 21 U.S.C. §351(a)(2)(B). On this score, there was ample evidence before the Grand Jury, quite independent of Mr. Howard's testimony, to support the charges lodged in the Indictment. As such, the defendants' motion to dismiss based upon this ground is denied. *United States* v. *DeLeo*, 422 F.2d 487 (1st Cir. 1970), cert. den. 397 U.S. 1037 (1970); *Coppedge* v. *United States*, 311 F.2d 128 (D.C. Cir. 1962) (Burger, J.).

IV. Motion To Exclude Certain Observations

"The defendants challenge the introduction, as evidence of CGMP violations, of various observations made at the Norwich sterile facility outside of the time frame during which the lots in issue were manufactured (e.g., T. 1603-1605; 2395; 2396-2400). While the Court has indicated that its verdict rests upon finding actual contamination, in violation of 21 U.S.C. §351(c), rather than a CGMP violation under 21 U.S.C. §351(a)(2)(B), it nevertheless feels compelled to briefly address this point.

"The Court is in agreement that, with respect to CGMP violations, the evidence must relate to conditions as they existed at the time applicable to the Indictment; that is, the time of manufacture of the lots in question. In proving its case, however, the Government should not be limited to use of testimony of observations actually made during the critical time period. Rather, it is proper to consider proof of conditions existing at times reasonably close to those in issue, providing that the Government can demonstrate that, by virtue of the nature of the conditions and the closeness in time, it is reasonable to infer that the same conditions occurred during the critical time period. *United States* v. *1,200 Cans, Pasteurized Whole Eggs, Etc.* 339 F. Supp. 131 (N.D. Ga. 1972). For example, while it is reasonable to assume that the physical layout of defendants' sterile facility was, for the most part, the same in June of 1973 as it was earlier that year, it is not necessarily proper to infer, without more, that because a wooden-handled tool was present in the sterile fill area in June, that it was also there in February. Likewise, while observations of many insects present in the fill room in June might be relevant as indicative of a continuing CGMP violation for improper insect-proofing, the mere presence of a single fly on one or more occasions cannot be used to infer the presence of insects at other times.

"Because the verdict as to Counts I and II was based upon actual adulteration rather than CGMP violations, and because the Court finds insufficient evidence of CGMP violations even considering all of the evidence now under challenge, it is unnecessary to rule upon the defendants' various objections falling within this category.

V. Conclusion

"In closing, the Court would like to express its deep appreciation to all of the lawyers who worked so diligently in preparing and presenting this case. The amount of time and effort which went into preparation of the case on both sides was apparent to this Court. The parties' efforts succeeded in enlightening the Court with regard to a rather complex and technical subject matter.

"The verdict stands as previously announced in court. The various motions upon which the Court reserved decision at different stages in the proceedings are resolved in accordance with the foregoing Opinion."

Thereafter, the corporation was fined $1,500.00. (F.D.C. No. 60004; S. No. 25-167G et al.; N.J. No. 30)

Penn Central Transportation Co. (a carrier with headquarters in Philadelphia, Pa.) and **CPC International** (a producer of bulk corn products with headquarters in Englewood Cliffs, N.J., and with a manufacturing plant at Pekin, Ill.), acting at Pekin, S. Dist. Ill.

Charged 2-17-78 by grand jury: when bulk corn gluten meal (Count 1) was shipped from Pekin, Ill., for delivery to Meadville, Pa., via the assigned railroad hopper car PR254567, and when bulk corn gluten feed (Count 2) was subsequently shipped for delivery to Augusta, Maine, via the same assigned railroad hopper car PR254567, the meal and the feed both contained the poisonous and deleterious substance lead oxide [which contrary to the car assignment had previously comprised an earlier cargo of that hopper car]; both the meal and the feed were unfit for food because of such substance, and both had been packed and held under insanitary conditions whereby they may have been rendered injurious to health; 402(a)(1), 402(a)(3), 402(a)(4). The carrier attempted to enter a plea of nolo contendere. Such a plea was rejected by the court. Both defendants pleaded not guilty.

The carrier moved to dismiss the complaint on the grounds that 21 U.S.C. 373 of FDA's statute (The Federal Food, Drug, and Cosmetic Act) excluded carriers, in the usual course of business, from 21 U.S.C. §§331, 333 and 342, because FDA's statute provided that "carriers shall not be subject to other provisions of this chapter by reason of their receipt, carriage, holding, or delivery of food . . . in the usual course of business as carriers"; that the carrier was subject to the Interstate Commerce Act and FDA's statute was intended to work in conjunction with the Interstate Commerce Act which already regulated carriers; that a compliance program had been established in 1975 to inspect food transport vehicles; that, in the 11 percent of cases where contamination was shown, it was not possible to tell how it originated; that generally, therefore, compliance by carriers should fall within the specialized knowledge of the Interstate Commerce Commission and not FDA. The carrier also moved to suppress from use at trial certain evidence obtained from the carrier. The government opposed both such motions by the carrier.

The case came on for trial by court and jury. CPC International was found to be not guilty as to both counts. Penn Central Transportation Co. was found guilty on Count 1 and found not guilty on Count 2. At sentencing, Penn Central Transportation Co. was fined $1,000 and was assessed costs.

Meanwhile, the carrier moved for a new trial, claiming, in part, that the jury's verdict was contrary to the weight of the evidence and was not supported by substantial evidence; that the court erred in not sustaining objections to questions in regard to an "assigned car" for lack of a foundation that the car in question was an "assigned car" on the date of the occurrence; and that the court erred concerning various jury charges. Similarly, the carrier moved for an acquittal and for an arrest of judgment, claiming, in part, that the court lacked jurisdiction because of the exemption of 21 U.S.C. §373, and that to hold the carrier and other carriers liable in view of the provisions in Title 21, Title 15, and Title 7 would make the exemption and suppression of evidence complete nullities and would be similar to a type of "entrapment." The court denied the carrier's motions (which appeared to the court to be on the grounds previously asserted, argued and decided adversely to the defendant).

After the court had assessed $6,865.86 costs against the carrier, the carrier moved to vacate such assessment. After a hearing, the court excluded various FDA expert witness fees and reduced the assessed costs to $2,493.16. (F.D.C. Nos. 60272, 60436; S. Nos. 26-137G, 96-447H; N.J. No. 31)

NOTICE OF JUDGMENT on Injunction Action

The Twin City Hospital, and **the Twin City Hospital Corp. of Dennison & Uhrichsville, Ohio,** and **James Z. Scott, M.D.,** president & medical director, **Eddie P. Sutkin,** administrator, **Charles W. Grandison,** laboratory director, and **Frank J. Wanosik,** assistant laboratory director, Dennison, N. Dist. Ohio.

Charged 7-23-75 in a complaint for injunction: that the defendants had been engaged at their hospital in Dennison, Ohio, in collecting, manufacturing, processing, testing, packing, labeling, storing and issuing bags of human whole blood and human red blood cells with anticoagulant (which had been shipped in interstate commerce), intended for transfusion; that FDA inspections revealed that the circumstances used for the collection, manufacturing, testing, packing, labeling, storage and disposition of human whole blood and human red blood cells were inadequate in a number of specified respects, and accordingly failed to conform with current good manufacturing practice; that the bagged blood and blood cells fell below the U.S.P. standards for quality and purity because they had not been manufactured in accordance with the biological products regulations; that the articles' labeling was false and misleading since it represented that complete Rh negative (CDE and Du) testing had been performed and the labeled results were final and conclusive, but in fact certain aspects of such testing (CE and Du) had not been performed at the time of labeling; and that the defendants were well aware that their activities were in violation of the law; 501(a)(2)(B), 501(b), 502(a).

A consent decree of permanent injunction enjoined the complained of violations and enjoined the continued storage and testing of such blood products at the defendants' blood bank except in a life saving emergency, unless and until a number of specific current good manufacturing practice methods, facilities and controls were found to have been established, operated and administered at the defendants' blood bank, and all the human whole blood and human red blood cells on hand were brought into compliance. A reinspection of the blood bank found it to be in compliance. (Inj. No. 706; S. No. 94-040H; N.J. No. 32)

NOTICE OF JUDGMENT on Miscellaneous Action

Sterility tests by FDA and information pertaining to laboratory controls, contamination, and design charges involving such tests, Washington, Dist. Columbia.

Charged 1-21-76 by Morton-Norwich Products Inc. (Norwich Pharmacal Co. Div.), Chicago, Ill., against HEW Secretary David Mathews and FDA Commissioner Alexander M. Schmidt: that the plaintiff had filed 39 requests for documents from FDA; that five of the requests (which were the subject of the plaintiff's action) sought copies of each FDA memorandum, record or document prepared between Jan. 1, 1965, and Oct. 15, 1975, pertaining to laboratory controls, contamination, and design charges involving FDA sterility tests; that FDA notified Norwich on Nov. 14, 1975, that additional time was required to determine its response to the plaintiff's requests; that on Dec. 3, 1975, FDA denied all documents requested by the above five requests; that Norwich filed an appeal with the assistant secretary for health requesting a review of each of the five denials; that, although Norwich had inquired concerning review of its five requests for information and had been advised by telephone that the bulk of the requested records would be denied, no decision in writing, as required by statute, had been received by Norwich within the specified 20 days; that the plaintiff was deemed to have exhausted its administrative remedies and had accordingly filed this action; that plaintiff prayed that defendants be enjoined from withholding the contested agency records which had been improperly withheld; that the defendants be ordered to produce such records; and that the court issue written findings determining that FDA's denials raised questions whether the agency personnel acted arbitrarily and capriciously. The government generally denied most of the plaintiff's charges. The plaintiff moved for summary judgment, as did the defendants. The court granted in part the defendants' motion for summary judgment authorizing any deliberative or policy material contained in the approximately 40 documents (which are the subject of the five requests in issue) to be withheld as exempt from compelled disclosure. The plaintiff's motion was also granted in part to the extent that within 10 days the agency had to reveal the fact later in the documents. In rendering such order, the court said:

"This is another Freedom of Information Act case. Following its now-settled practice, the Court requested the Government agency to submit samples of the documents for which exemption from disclosure is claimed in order to focus the issues in an adversary context. This was done, aided by some discrete excerpting, and the controversy was briefed and argued.

"At stake are some 49 documents out of hundreds requested and disclosed following an elaborate file search and administrative clarification of what was sought. The documents still in controversy are claimed to be exempt under (b)(2) and (b)(5), 5 U.S.C. §552. The claim of exemption is supported by an affidavit from a responsible, informed official. Appropriate indices were furnished, together with the sample documents. The parties cross-moved for summary judgment. There is no factual dispute. The Court must accordingly attempt to interpret what the Freedom of Information Act means when applied to the circumstances of this case.

"Three requests of plaintiff are still opposed by the agency and form the basis of this litigation. The first contested request seeks: 'a copy of each memorandum or other record or document relevant to the controls and procedures utilized between Jan. 1, 1965, and Oct. 15, 1975, to eliminate possible laboratory contamination in the facilities operated by or on behalf of the Food and Drug Administration for the performance of sterility tests.' Two categories of documents within this request have been withheld: (1) worksheets showing quality assurance sterility sample results of analyses conducted in 1972 and 1974 on 'audit' samples, and (2) inter-agency memoranda containing selective portions of the results of the samples, analyses of the results, and recommendations for changes in laboratory operation, analytical

procedures and/or additional training.

"Plaintiff's second request seeks to obtain a copy of each memorandum or other record or document prepared between Jan. 1, 1965, and Oct. 15, 1975, pertaining to the need or desirability of changes in the design, construction materials, structure, or equipment in facilities operated by or on behalf of the Food and Drug Administration for performing sterility tests. Included in these documents are specific cost estimates supporting the budget needed to make proposed changes. A sample was again provided.

"The final dispute concerns plaintiff's request for: 'a copy of each memorandum or other record prepared between Jan. 1, 1965, and Oct. 15, 1975, pertaining to the need or desirability of changes in the sampling and laboratory procedure in use by each laboratory of the Food and Drug Administration for testing (a) sterile impregnated gauze pack and/or (b) other sterile products.' Three classes of documents are within this request. First, there are 23 intra-agency memoranda reflecting the on-going pre-decisional deliberations of, summaries of meetings by, and correspondence between the members of, an internal FDA working group known as the Task Force on Sterility. No representative sample is provided, but the memoranda have been clearly indexed. Also withheld are memoranda containing discussions of possible modifications of analytical procedures and controls utilized in performing sterility testing. A sample document has been made available. Finally, the agency refused to reveal two interagency memoranda containing recommendations of personnel from the Center for Disease Control of the Public Health Service and the Food and Drug Administration concerning a draft set of Good Manufacturing Practice regulations (GMPs) for large volume parenteral products.

"The defendants claim exemption under (b)(2) and (b)(5) for the first category and again invoke a (b)(5) exemption as to all the other requests in dispute as summarized above.

"Certain benchmarks, well established by prior decisions, serve as initial guides in interpreting and applying the statute. A person requesting information is not required to show a need or a reason, and an agency must disclose wholly useless, meaningless and misleading information unless it is exempted. Where exemption is claimed, as here, the exemption must be narrowly construed, and the burden of proof is on the agency, *e. g., Washington Research Project, Inc.* v. *Department of Health, Education & Welfare, 164* U.S.App. D.C. 169, 504 F.2d 238, 244 (1974), *cert. denied,* 421 U.S. 963, 95 S.Ct. 1951, 44 L.Ed.2d 450 (1975). Against this background, the Court turns to the specific requirements of the exemption.

"The Court finds that (b)(2) does not support the agency's refusal to release documents in the first category. The material relates neither to minor or 'housekeeping' matters nor predominantly to internal personnel rules and practices of the agency, but rather to the substantive performance, and competence of the FDA in this area. Moreover, plaintiff has agreed to the deletion of the names of both the employees tested and the employees' supervisors, and therefore the aspects of the documents which might otherwise relate to personnel practices have been eliminated. Accordingly, under the opinion of either Judge Wilkey or Judge Leventhal in *Vaughn* v. *Rosen,* D.C.Cir, 523 F.2d 1136 (1975), the (b)(2) exemption is not available.

"It remains to consider the (b)(5) claims as to all of the materials in controversy.

"The Court has before it here primarily documents that recommend or are, as in the case of the Task Force papers, clearly developed in aid of a recommendation. Thus the papers are unquestionably an integral part of the agency's deliberative processes. All of the documents fall directly under the (b)(5) exemption, and the agency may refuse to produce any material that contains opinions, advice, evaluations, deliberations, policy formulations, proposals, conclusions or recommendations. The issue is whether factual statements found in these deliberative documents must be disclosed or also treated as exempt along with the rest of the text. If this proposition were presented as a matter of first impression, the Court would favor a rule of thumb to the effect that any document containing an explicit recommendation and legitimately prepared in the regular course of the agency's business to further its deliberative process is exempt in its entirety. It appears that Congress could rationally have so intended, recognizing the overriding need to encourage the free exchange of ideas within the Government during deliberations and policymaking.

"The United States Court of Appeals for this Circuit has, however, taken a different approach. It has narrowed the exemption and required that even purely deliberative documents be excerpted under certain conditions to disclose facts stated within the four corners of the documents. . . . The task presented here therefore is to specify what statements of fact must be disclosed as outside the exemption after censoring the deliberative document of its policymaking features. In the present state of the law the Court of Appeals has understandably given only the most general indication of its point of view. In view of the infinite variety of documents that the Freedom of Information Act covers and the equally great variety of procedures followed by Government agencies in formulating policy, the case-by-case development of the meaning and effect of exemption (b)(5) has left many unanswered questions and much uncertainty. The Court of Appeals has suggested certain general tests: Is the fact 'easily severable'? Is the fact 'inextricably intertwined'? Is the fact contained in a 'summary' that has become part of the deliberative process? Is the fact already in the 'public domain'? Is the fact purely 'investigative'?

"It is necessary in this case to give these tests a clearer definition so that disclosure, where appropriate, may proceed. It appears to this Court that the rules stated immediately below must be followed in separating fact statements from their deliberative context in the case of the documents here in controversy.

"A fact is 'easily severable' if it is in a separate sentence and is deemed 'inextricably intertwined' only if it is stated along with nonfactual material in a single sentence. Since almost all statements of fact are summary in the sense of being incomplete and the inclusion or emphasis of a particular fact is necessarily a matter of judgment, a statement of fact contained in a separate sentence or sentences may be withheld as exempt even if a part of the deliberative process only (1) when it appears from the face of the document that the writer is intentionally purporting to summarize facts, and (2) the facts have already been made public by the agency or may be elsewhere ascertained from other documents available from the agency by operation of the Act.

"The Court is aware that this places a heavy burden on the responding agency but the difficulty is largely of the agency's own making. There is nothing in the Freedom of Information Act which requires an agency to claim an exemption. It is also obvious from the experience under the Act that much material for which exemptions are now being claimed has no current value or significance whatsoever. Demands are being made for disclosure of documents that go far back in time and which truly have lost any practical consequence. Indeed, it is difficult to understand why the Government has preserved many of these papers. If an agency takes a more liberal attitude about its relations to the public it can proceed by disclosing much of the exempted material without damage to the public interest or creating precedent which will injure its interests. A more enlightened policy would be one that asserted exemption only when genuinely important. This would greatly reduce the ever-growing burden on the Federal Courts and would also reduce the expense of attorneys' fees assessed in these cases against the Government. Most importantly, such an approach would

promote the purposes underlying the Act and bring about a far healthier understanding of governmental process. Thus the agency has it within its own hands to minimize greatly the need for excerpting and reviewing sentence-by-sentence papers that intermingle fact and policy.

"One issue remains. Counsel for plaintiff urges that the Court examine each disputed document *in camera* and make the determinations as to what is fact and what is not. . . . This Court has elsewhere expressed some of the considerations which have led it to reject *in camera* proceedings. . . . In the present instance, these same reasons, plus other considerations, again prompt the Court in its discretion to reject *in camera* review of the designated documents.

"The principal reason advanced by plantiff in urging *in camera* consideration is that courts are to be trusted to be impartial and that a third-party review by a court is more comforting than review by representatives of the agency resisting disclosure. This is superficially enticing if one overlooks the experience of history that indicates how arbitrary judges as well as others in authority become if they conduct their business in secrecy. But apart from this danger, which plaintiff recognizes, it is necessary to point out two countervailing considerations. First, if the Government wished wrongfully to withhold, it need not have ever indicated that the documents existed in the first place. Second, sanctions now exist under the amended Act against those who improperly conceal, 5 U.S.C. §552(a)(4)(F). The FDA processes thousands of Freedom of Information Act requests a year. It has a specialized staff which proceeds with legal advice. The U.S. Attorney in contested cases reviews that advice. There is nothing in this case to suggest that the agency has not been forthright or responsible. The Freedom of Information Act must proceed in an atmosphere of confidence in government. If the agency cannot be trusted, the Act will never work. It is a profound mistake to transfer administrative responsibility to judges on the theory that persons employed by the Executive branch are not honest or lack judgment. The effort to do this through the *in camera* process is misplaced.

"Defendants' motion for summary judgment is granted in part and any deliberative or policy material contained in the documents may be withheld as exempt from compelled disclosure. Plaintiff's motion is granted in part to the extent that within ten days the agency must reveal the fact data in the documents as directed in this opinion."

Thereafter, the defendant moved for clarification or to amend the court's order, so as to delete the identity and location of the FDA laboratories from the laboratory work sheets showing quality assurance sterility sample results of 1972 and 1974 "audit" analyses. Upon consideration of such motions, it appeared to the court that in conformity with the Freedom of Information Act, the identity and location of the FDA laboratory could and should be disclosed, and the court denied the defendant's motions and ordered that its previous order should stand without amendment. Meanwhile, the plaintiff made various objections concerning the documents that the defendants produced. Ultimately, however, in a Northern District of New York criminal action, in response to a motion by Morton-Norwich to compel discovery and inspection of the documents covered by the court's order in this case, complete copies of all the documents were released to the defendants. (Misc. No. 328; N.J. No. 33)

Notices of Judgment are given pursuant to section 705 of the Federal Food, Drug, and Cosmetic Act. Notices of Judgment report cases involving seizure proceedings, criminal proceedings, and injunction proceedings. Seizure proceedings are civil actions taken against *goods* alleged to be in violation, and criminal and injunction proceedings are against *firms* or *individuals* charged to be responsible for violations. The cases generally involve foods, drugs, devices, or cosmetics which were alleged to be adulterated or misbranded or otherwise violative of the law when introduced into and while in interstate commerce, or while held for sale after shipment in interstate commerce.

Notices of Judgment are prepared by Food and Drug Division, Office of the General Counsel, HHS.

Published by direction of the Secretary of Health and Human Services.

Arthur Hull Hayes Jr., M.D., *Commissioner of Food and Drugs*
Washington, D.C., Sept. 1, 1982

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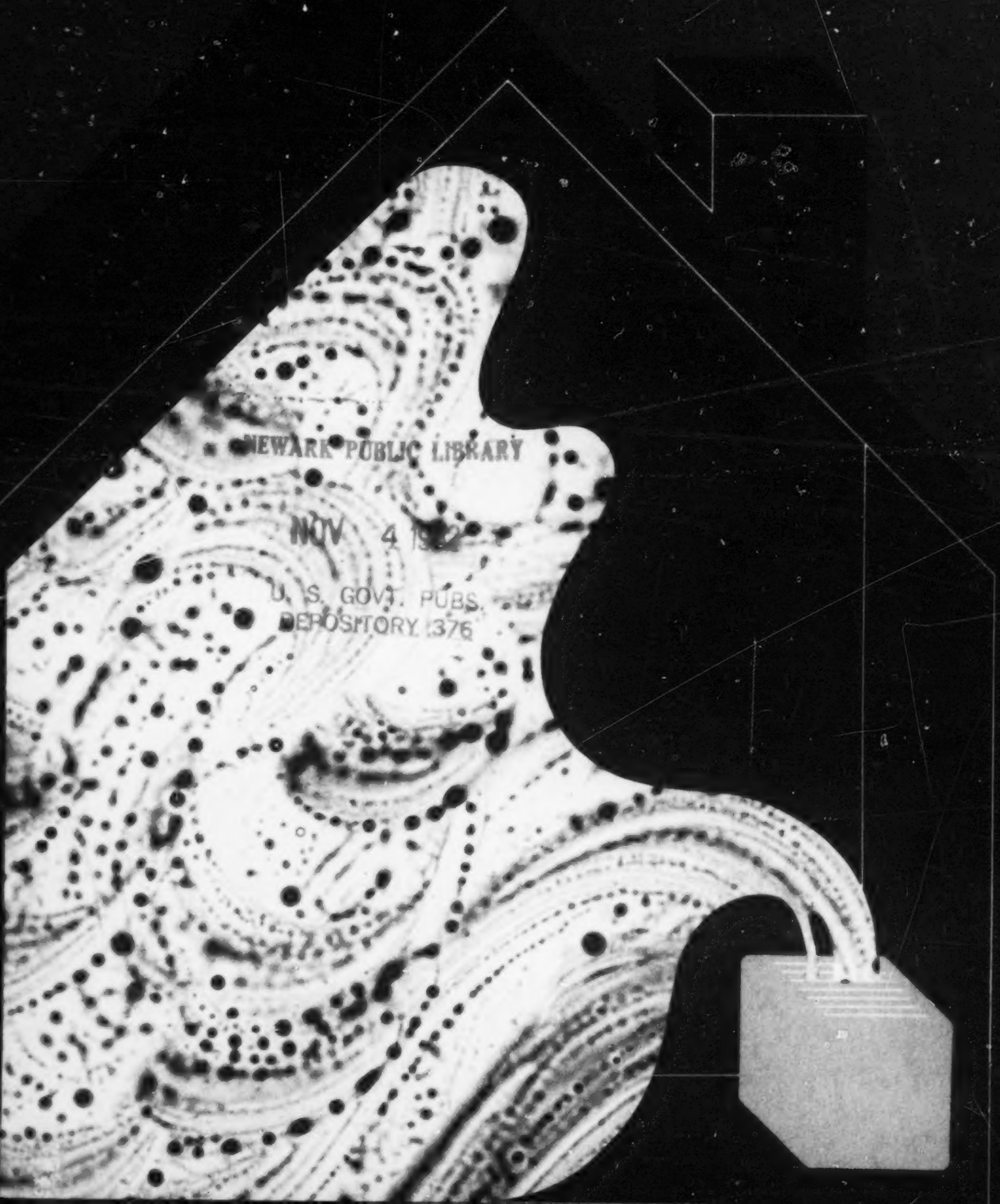
The Cans And Can'ts Of Air Purifiers



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FDA CONSUMER

VOL. 16 NO. 8 OCTOBER 1982

The Cans and Can'ts of Air Purifiers 5
Everybody would like to breathe perfectly clean air, indoors or out, but that's pretty impracticable. For those who need cleaner indoors air for bona fide medical reasons, there are air-cleaning devices that can help under specified conditions, but it's a tricky market.

For Food Labels, Better Read = Better Fed 8
Honing up for its program to design a new nutrition labeling format that people can understand and use, FDA plans to test several design ideas on, of all persons, people. Hearings will also be held to solicit suggestions.

FDA's New Code: A Clean Sweep for Food Stores 12
Model code for food retail store sanitation will give food stores uniform standards to go by and, upon adoption by state and local governments, will provide universal criteria for enforcement.

The Thyroid: More Than a Pain in the Neck 14
One of the best known of the body's glands, the thyroid is all-important in maintaining the delicate balance needed in metabolic and related activities.

Reye Syndrome Spells Caution to Parents 18
Reye syndrome is a dangerous complication that occurs mostly in children when recovery from such viral diseases as flu and chicken pox sometimes goes awry. The syndrome may be associated with the use of certain medicines.

Excipients Give Drugs Versatility 22
The bulk of ingredients in many drugs consists of non-active materials called excipients that make the drugs adaptable for desired uses. Excipients also perform a great many other functions needed for medicines.

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Acting on the premise that the label ought to tell the shopper what he needs to know about a food package's contents, and no more, FDA is having a new look at the nutrition information part to make sure it's useful, and understandable. Over the next several months the agency will be considering new ways of getting nutrition information across to the consumer. See For Food Labels, Better Read = Better Fed, *beginning on page 8.*

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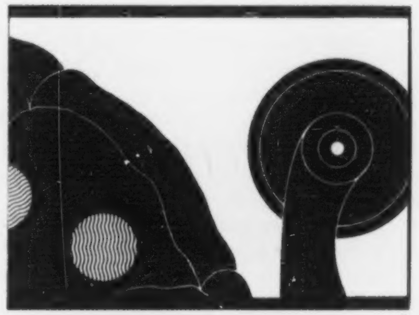

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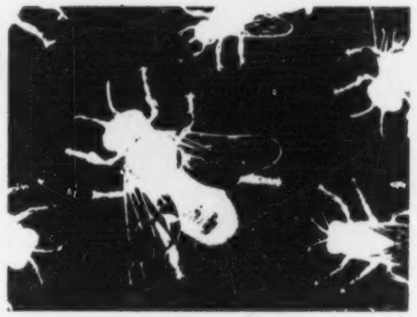

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Updates

Drug Standards Offered

FDA has moved one step closer to the adoption of standards for four categories of non-prescription drugs. On July 9, the agency published proposed monographs spelling out the acceptable ingredients and labeling for topical antimicrobial drug products, anticholinergics, expectorants, and drugs to aid in earwax removal.

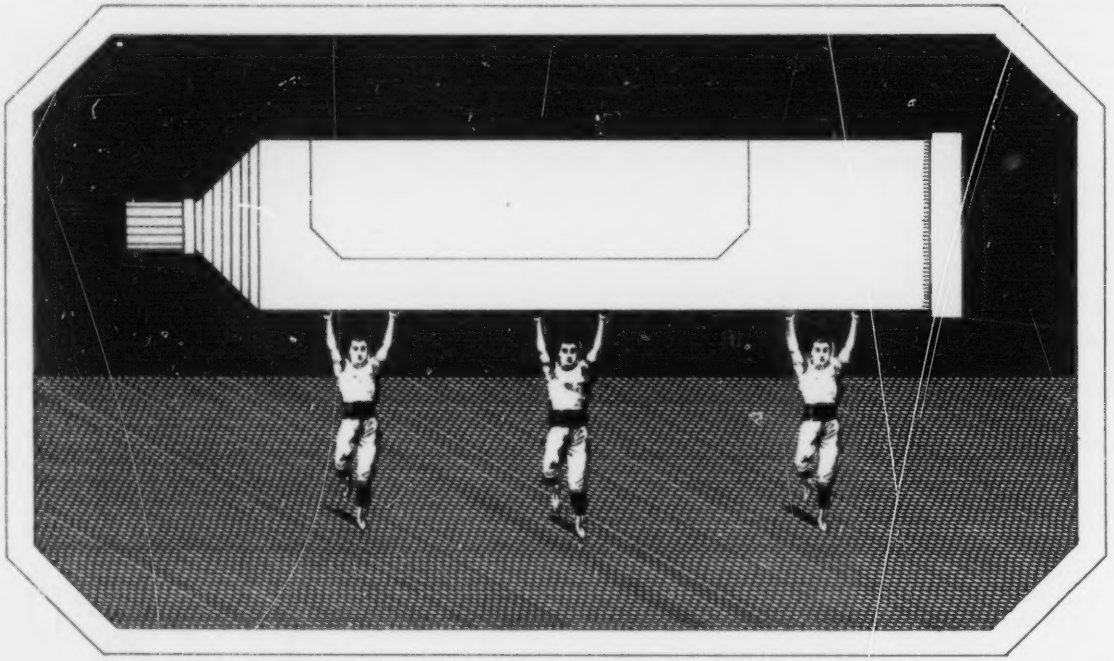
The agency's decisions were based on its evaluation of recommendations by advisory panels of non-government experts and of public comments on these recommendations.

The proposed monograph for topical antimicrobial drug products differs slightly from the recommendations of the Advisory Review Panel on Antimicrobial II Drug Products. FDA includes neomycin sulfate among the ingredients considered safe and effective, although the panel had called for additional testing because of its belief that some people may become allergic to this drug through repeated use. Added by FDA to the list of safe and effective ingredients is bacitracin zinc, which had been omitted inadvertently from the panel report.

Both the agency and the panel agreed that the following ingredients are safe and effective as topical antimicrobials: bacitracin, chlortetracycline hydrochloride, oxytetracycline hydrochloride, tetracycline hydrochloride and polymyxin B sulfate when used in combination with other antibiotics. Gramicidin needs additional testing, according to both FDA and the panel.

The panel established two categories of topical antibiotic drug products—skin wound protectants and skin wound antibiotics. FDA combines these into a single category called "first aid antibiotic." The approved indications for use of these products is "First aid to help prevent infection in minor cuts, scrapes, and burns." The word "scrape" has been substituted for the panel's harder-to-understand term "abrasion."

Warnings and directions for use have been simplified in FDA's proposed monographs. For instance,



in all of them "doctor" is used instead of "physician," and "warning" replaces "caution" as a signal word to alert consumers to important information. In the topical antimicrobial monograph, the phrase "Stop use and consult a doctor if the condition persists or gets worse" takes the place of the panel's recommended warning against use of the product "if itching, redness, swelling or pain develops." These are the very symptoms topical antimicrobial products are used to treat, FDA says.

(More on what the advisory panel had to say can be found in the article "Panel Reports on First Aid Ointments" in the March 1977 *FDA Consumer.*)

Anticholinergics (drugs that help stop runny noses and watery eyes) and expectorants (drugs used to help remove secretions from the respiratory tract) were included in the report of the Panel on Cold, Cough, Allergy, Bronchodilator and Antiasthmatic Drug Products. (See "The Common Cold: Relief but No Cure" in the September 1976 *FDA Consumer.*) FDA is issuing the proposed monographs for these products in segments. Anticholinergics and expectorants are the first; the others will be published later.

The agency agrees that there are no safe and effective ingredients in either category of drug products and accepts the panel's recommendations identifying those ingredients that are not safe and effective and those that need further testing. *Atropa belladonna* (Deadly Nightshade) and *Datura stramonium* (Thornapple, or Jimson Weed) should not be allowed in anticholinergic products, according to both FDA and the panel. Both also said that antimony potassium tartrate, chloroform, iodides, squill preparations and spirits of turpentine as an oral drug don't belong in expectorants. Atropine sulfate and belladonna alkaloids need further testing as anticholinergics, as do such ingredients as ammonium chloride, beechwood creosote, eucalyptol and pine tar preparations if they are intended for use as expectorants.

In the event some ingredient is found safe and effective for either of these uses, the panel recommended labeling. In its proposed monograph, FDA has made a few changes in this labeling. "Dizziness" was added as a reason for discontinuing use of an anticholinergic, and the word "high" was deleted in describing a fever in the warnings section of the expectorant monograph. The agency believes it is important for consumers to recognize the presence of fever whether it is high or low.

As to otic (ear) products for use in aiding the removal of earwax, FDA agreed with the panel recommendation that carbamide peroxide in anhydrous glycerin is safe and effective for this purpose and that benzocaine is not. But the agency disagreed with the classification of glycerin as safe and effective, recommending instead that additional testing be done on this ingredient.

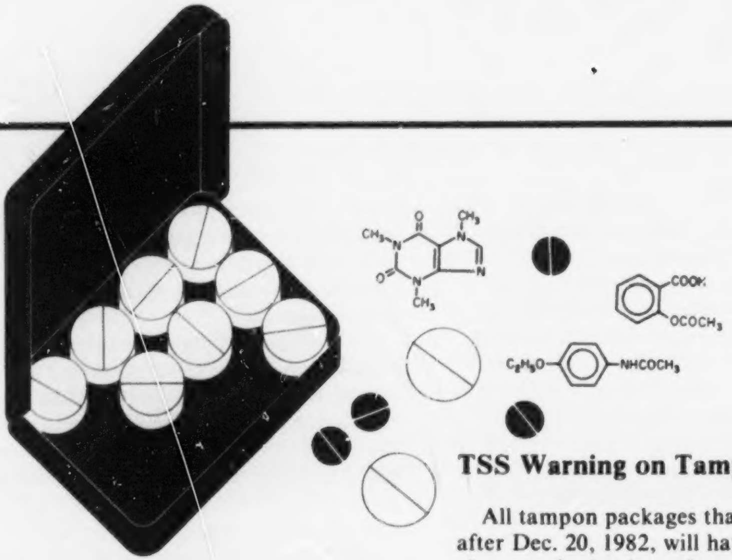
The otic drug product panel said these products should be called "earwax softening agents." FDA prefers "earwax removal aid." Other labeling changes made by FDA include use of the term "excessive" instead of "obstructive" in describing persistent earwax, and substitution of the phrase "**For use in the ear only**" for "For external use only; not to be swallowed" in the directions-for-use section. (The many things the panel had to say about ears and earwax removal were discussed in "Now Hear This" in the December 1977-January 1978 issue of *FDA Consumer.*)

All three proposed monographs (anticholinergics and expectorants are combined in one document) were published in the July 9, 1982, *Federal Register.* Manufacturers have been allowed a year to present any new data in these categories of non-prescription drugs, and public comments on such data will be accepted until September 1983. Final monographs will be published after all data and public comments have been reviewed. Manufacturers will have 12 months after that date to revise labeling and reformulate their products, if necessary.

No More "P" in APC

Phenacetin, the "P" in APC pills, will not be allowed in either prescription or non-prescription drugs after Aug. 10, 1983, according to a recent FDA proposal. The agency took this action because phenacetin can cause kidney damage and anemia in persons who ignore label directions and take too much of the products or take them for too long. There have been reports of injuries and even deaths.

(Continued following page)



In a notice in the Aug. 10 *Federal Register*, FDA said that any prescription or non-prescription drug products containing phenacetin will be unlawful a year after that date.

Widely used as a painkiller for over 80 years, phenacetin is always found in combination with other ingredients, such as the aspirin and caffeine in APC compounds. The history of abuse from the misuse and prolonged use of phenacetin led FDA in 1964 to require the following statement in the labeling of all phenacetin-containing preparations: "Warning—This medication may damage the kidneys when used in large amounts or for a long period of time. Do not take more than the recommended dosage, nor take regularly for longer than 10 days without consulting your physician."

In 1977 an advisory panel on over-the-counter analgesic products cited phenacetin's potential for causing kidney damage and blood disorders. Large doses, over a long time, can also result in life-threatening kidney disease and possibly cancer of the kidney and bladder, the panel reported, recommending that phenacetin's use in non-prescription drugs be prohibited. The panel's report on all non-prescription pain-killing drugs was discussed in "Painkillers: Their Uses and Dangers" in the September 1977 *FDA Consumer*.

Most of the products that contain phenacetin can be readily reformulated, FDA said. Many have been reformulated already, in response to the advisory panel's report. Instead of phenacetin, aspirin or acetaminophen can be used. Both have similar pain-killing and anti-fever qualities.

TSS Warning on Tampons

All tampon packages that go on the market on or after Dec. 20, 1982, will have to include information about toxic shock syndrome, a rare but serious, and sometimes fatal, disease associated with tampon use. A new regulation, published by FDA in the *Federal Register*, requires either a comprehensive statement on the package or a shorter alert advising users to read an information leaflet about the disease that is included in the package.

The shorter alert reads: "ATTENTION: Tampons are associated with Toxic Shock Syndrome (TSS). TSS is a rare but serious disease that may cause death. Read and save the enclosed information."

The longer statements on or in the tampon package are to include information on:

- The warning signs of TSS—sudden high fever (usually 102 F or more) and vomiting or diarrhea. (Other signs may include fainting or nearly fainting when standing up, dizziness and a rash that looks like sunburn.)
- What to do if these signs appear—remove the tampon at once and seek medical help right away.
- The incidence of TSS in women, and the higher risk among those under 30 and teen-age girls, and the risk of death.
- The advisability of using tampons with the least absorbency needed. (One study has indicated that the risk of TSS appears to be smaller with less absorbent tampons.)
- The avoidance of the risk of tampon-related TSS by not using tampons, or the possible reduction of risk by alternating tampons with sanitary napkins during menstrual periods.
- The need to seek medical attention before again using tampons if TSS warning signs have appeared in the past.

The Cans And Can'ts Of Air Purifiers

by Harold Hopkins

Public concern about polluted air has given a push to the fortunes of companies selling air-cleaning or purifying devices designed to be used indoors. The most noticeable beneficiaries—no doubt because their prices are as modest as some of their promotion is immodest—are the ones who offer small tabletop or personal units.

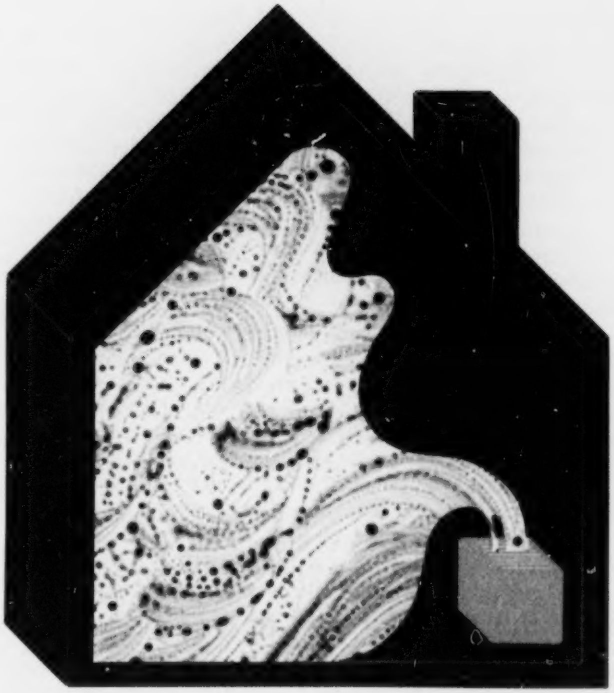
These compact and convenient units can be carried from room to room, to the office or elsewhere. Their portability enables the user to carry his or her protection along, as far as an extension cord will take it. Their popularity is ample evidence that people think they're getting something beneficial for the $20 or more put into them.

Sales for these little gadgets have remained strong for a couple of decades now and show no sign of letting up. However, when claims for such devices edge over into that rich trade territory having to do with human health, FDA may interpose a dampening note. Health claims can make a device a medical device subject to regulation by FDA.

Claims for air cleaners say they'll scrub a room's air of large or small particulates such as dirt, dust, pollen, tobacco smoke, soot, dog and cat dander, lint, hair, and mold spores and irritating or undesirable odors and chemical fumes or gases. A few may claim the capability to eliminate harmful bacteria and viruses. No matter. Such a statement does not constitute a therapeutic claim and is not a cause for FDA action. Some of the desk top or coffee table models have chemical inserts that waft a pleasing scent of lemons toward the owner, who may associate this fruit with freshness. Perfumed aerosol sprays or other deodorants are not regarded as air cleaners, and in a sense might be said to have the opposite effect.

Modern man seems almost inherently obsessed with finding a machine that will do his dirty work—or at least cover it up. But when it comes to indoors air, there's an awful lot of it, and extraction of all the impurities from it is no breeze, even in this age of computer chips and other gizmos that do practically everything.

This is not to say that aspiring to clear a room's air of its floating contaminants is an unattainable quest. There are devices that can do a pretty good job, but they're effective only under certain conditions.



The kinds, sizes and amounts of impurities that can be removed from a roomful of air vary. It depends on a number of factors, including the type of air cleaner and its efficiency and capacity; the nature and quantity of the particulates to be removed; the amount of loose particles on floors, walls, ceilings and furnishings that can become easily airborne; and the rate new air is coming into the room via regular air inlets, room leaks, open doors, etc.

Most air cleaners intended primarily to clean the air for breathing purposes are of the recirculating type. A recirculating air cleaner continually pulls air through a filter or filters or other entrapment units. Recirculating air cleaners should be capable of pulling air through their filters at a faster rate than the supply of new air entering the room. The volume of air a fan can handle is rated in cubic feet per minute displacement, or CFM. A recirculating device may be capable of funneling the entire volume of air in a room through its filters several times every hour. If the air cleaner's fan fails to generate enough air current to draw floating particulates into the filter from the far sides of the room, it's not really very effective. In a bedroom, the closer the filter's downstream side is to the sleeper's nose, the cleaner air he or she will breathe. Air cleaners differ mainly in methods of trapping particulates or other impurities and in the array of entrapment components used. Some incorporate two or more entrapment units, arranged in stages that first catch the larger or bulkier particulates on the coarser screens or filters. This is intended to keep the larger particles from quickly clogging or loading up—and requiring more frequent replacement of—the more expensive filters with finer pores or openings that catch the smaller particles in the final stage.

The best known entrapment method is the mechanical filter. It consists of one or more removable sheets, blankets or screens that are made of glass fibers, fabric, plastic, wood, metal or other materials. These filters have tiny openings or pores small enough to capture particulates as air is forced through them. A filter's size is normally given in square inches.

The most highly regarded mechanical filter is the HEPA (high efficiency particulate air) or "absolute" filter. This filter can also be coated or imbued with chemicals that kill molds, bacteria or viruses borne on dust particles, once they're caught by the filter. The HEPA filter is composed of a mixture of various sized glass (boro-silicate) fibers. It was developed and perfected by the military during World War II and used by the old Atomic Energy Commission after the war for filtering out radioactive dust and other airborne radioactive contaminants.

HEPA or absolute filters are used in a large number of medical, military, electronic and industrial applications where clean air—even "superclean" air—is essential to the work. Such uses include electronics manufacturing, computer operations, missile aiming and guidance systems, parenteral and other drug formulation plants, and hospital isolation wards for burn patients. At least two air cleaner manufacturers who have registered their products as medical devices with FDA use the HEPA filter.

An ultraviolet radiation chamber is used in some air cleaners to kill molds, bacteria and viruses. The UV radiation is emitted from lamps in a shielded chamber to bathe the air passing through. One company that offers it says the UV chamber is shielded to prevent the escape of the toxic gas ozone, produced by UV radiation. FDA prohibits the marketing of any medical device that emits more than 0.05 parts ozone per million parts of air circulating through the device. At one time, devices with UV lamps that produced ozone were marketed with claims of effectiveness as a room deodorant. FDA and others counter that the ozone merely paralyzes a person's olfactory nerves, deadening the sense of smell. Such ozone devices are no longer on the market.

Chemical filters act upon chemical substances in the air, including ozone and many other gases, vapors and irritants. The best known chemical filters are made of activated carbon or charcoal, which removes certain offending chemicals by adsorption—that is, causes them to be deposited on the charcoal's surface area. Other types of chemical filters contain potassium permanganate or similar substances that react with various chemical air contaminants to bind them up or neutralize them.

Mechanical and chemical filters are not economically reusable. When a filter gets loaded with contaminants, it is less effective and should be replaced.

Another air-cleaning system involves electrostatic precipitators (sometimes called electronic agglomerators). These do not have a filtering function. They work by placing a negative charge on particles in air entering the cleaner. The particulates are then attracted and held fast by a positively charged plate, grid or screen. These units are reusable, and when loaded with particulates may be cleaned in a dishwasher or with a vacuum cleaner. Electrostatic precipitators may be installed in air-conditioning systems.

There is another air-cleaning device on the market called a negative ion generator which, its promoters have claimed, increases the ratio of negative to positive ions in a roomful of air. An ion is an electrical charge. The generator works by producing negative ions, which are dispersed into the room and combine with particles in the air, imparting a negative charge to them. These charged particles are then attracted to and held by walls, floors, etc., which carry a positive charge. Some makers have claimed that the preponderance of negative ions in a room from this generation has a beneficial health effect. FDA has challenged claims that negative ions have a beneficial health effect, stating that the agency has seen no valid evidence of such an effect.

Making decisions about whether to buy an air cleaner, and the kind to buy, calls for some basic considerations.

The first is that a person who doesn't remain all the time in one spot, such as a bedroom in the house, cannot benefit the entire day from an air cleaner. Therefore, choice of the place to put the device for the best benefit is important.

Need is another major consideration. It's obvious that even if no medical claims are made for an air cleaner, the potential purchaser is almost bound to associate health as well as comfort with anticipated benefits. Nevertheless, it's practically impossible for a layman to judge the exact value of cleaner air to health and to clearly identify the contaminants, if any, that may be causing trouble. A person who feels that a particular condition could be helped by an air cleaner should consult with a doctor to determine actual need.

There may be some surprises. In the case of a patient allergic to ragweed pollen, for instance, a doctor may decide that an air cleaner promises no substantial benefit—that staying indoors as much as possible during the ragweed pollen season is the best thing to do, since ragweed pollen grains are rather large and don't travel far when airborne (of course, smaller pollen may also be associated with individual allergies). For another condition, a doctor may decide that air conditioning to reduce moisture or to lower air temperatures is what the patient needs. A doctor may be able to tell the patient just what results he or she might expect from an air cleaner to justify the purchase, and may be able to recommend a particular kind or model that's best for a given patient's condition.

The prudent purchaser should remember that a lot of air has to be forced through an efficient filtering system in a controlled air space for any air cleaner to clear the air of its burden of particulates. It should be plain to the careful purchaser that any contrivance powerful and effective enough to clean up a roomful of air is not going to come cheap and will not likely fit handily on a coffee table. Common sense and some quick calculations will tell most that it's impossible to remove all the particulates from an entire roomful of air with a device that has only a low-powered fan or a coarse filter a few inches wide, or both.

If an air cleaner's labeling makes therapeutic claims (for instance, that it will cure or alleviate illness, protect against infections, prevent lung cancer, halt asthma attacks, put an end to allergic reactions, reduce emphysema symptoms or ward off a cold), FDA's Bureau of Medical Devices is ready to examine the claim and challenge any overreaching. If there are medical or health claims on the labeling, FDA regards the air cleaner as a medical device subject to regulation under the Federal Food, Drug, and Cosmetic Act. The manufacturer or distributor is responsible for assuring that the product will perform the therapeutic function claimed, and must furnish adequate directions to the purchaser for safe and effective use. Medical air cleaners are designated as Class II devices, meaning they have to meet performance standards FDA may set that will assure safe and effective use. Although the agency has not yet set such standards for air cleaners, it does have regulatory authority over the labeling for them.

Examining the advertising of household products such as air cleaners and seeing that the representations don't get out of hand is a responsibility of the Federal Trade Commission. FTC's staff will examine the claims in terms of the functions named in the advertising. If such advertising states that an air cleaner is offered for a specific medical or therapeutic purpose, FDA has the authority to require that adequate directions be furnished to enable the purchaser to use it safely and for the purpose offered for sale.

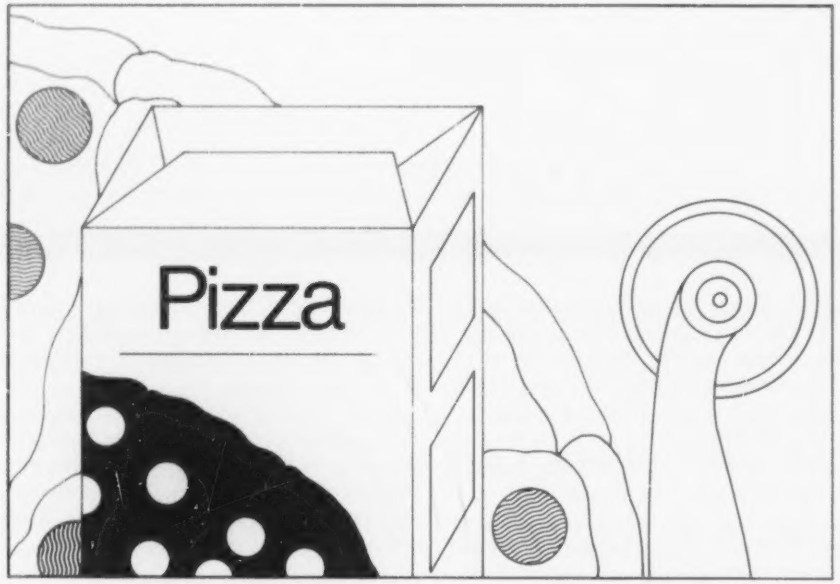
Although some air cleaners are intended for the individual home user, others on the market are intended mainly for industrial, commercial, hospital and business uses, and make no medical claims, even though some do in fact remove general or specific contaminants that may be harmful to health.

The pertinent method of testing the efficiency of air filters for breathing purposes is the hot DOP (dioctyl phthalate) test, which is essentially a "count" of tiny, liquid dioctyl phthalate particles artificially produced by the use of heat. They are introduced into and suspended in samples of air. These samples are measured immediately before and after passing through the filter and the results compared. Measuring is done by a photo-multiplying tube that senses the light-scattering effects of the particles in a beam of light. One brand of HEPA filter, for which claims are made of catching particles down to a size of three-tenths of a micrometer, or micron (about 1/25,000th of an inch), rates as 99.97 percent efficient by this test. Particles as small as three-tenths of a micrometer include bacteria, cigarette smoke and metallic fumes. Pollens, molds and normal atmospheric dusts range upward in size, five to 10 micrometers, for instance. Other particulates are still larger.

There are other types of tests for air filters, based on weight and staining properties of air particles of importance to building cleaning and maintenance. A person considering the purchase of an air cleaner to improve breathing conditions might appropriately ask its manufacturer for the DOP rating of the filter(s) used, in conjunction with the fan's CFM rating or power, the filter's CFM capacity, and the space dimensions recommended for using the device. This can also help purchasers avoid overkill—that is, buying more air cleaner than they need.

Harold Hopkins is editorial director of FDA Consumer.

For Food Labels, Better Read = Better Fed



by Chris Lecos

The next time you pluck a can or package of food from your kitchen shelf, take a good look at the nutrition label and then ask yourself: How much of this do I *really* understand? What don't I understand? What's on this label that really interests me? What doesn't? What would I rather see or be told about this food product? How would I like to see it told?

Over the last four years, the Food and Drug Administration has gone to America's food shelves to have another look at nutrition labeling in an attempt to find answers to these kinds of questions on behalf of the food-buying public.

FDA's goal has been to find out if the current nutrition label is adequately serving the public's needs and interests. The consensus—after extensive research and study—is that the public is not being well served. Instead, many consumers consider the present label confusing, hard to understand and, in part, too technical. Further, the present labeling may be loading many consumers with more information than they can use or want. Finally, consumers generally prefer a label that tells them what they should avoid or not overconsume.

From what FDA has learned, the agency is now trying to develop a more meaningful nutrition label. In the near future, the agency will take a number of selected consumers and, through sophisticated testing equipment and follow-up interviews, measure their reactions to a variety of new labeling formats. The new labeling ideas were prepared for FDA by a professional package and design firm, Robert P. Gersin Associates of New York City.

The research will take 12 to 18 months, according to Raymond C. Stokes, head of the Division of Consumer Studies in FDA's Bureau of Foods. FDA is planning additional public hearings to solicit comments and ideas from industry, nutritionists, consumers and others, and the agency also hopes to see various labeling formats market-tested. Out of all of this, FDA hopes to come up with a nutrition label format that will be simpler, clearer and easier to understand—one that presents accurate information, satisfies a broader range of consumer interests, and yet is acceptable and not costly to the food industry.

Deciding what to put on a nutrition label is no simple task. First, people's

Proposed Formats for Consumer Testing

The nutrition labels shown here include the design currently being used plus some of the new formats proposed by Robert P. Gersin Associates. In the new formats there is more emphasis on calorie and sodium content, and RDAs are given for only four vitamins and minerals instead of seven. In Format B word descriptions are used instead of percentages to rate vitamin and mineral content. In Format C the percentage of vitamins and minerals is emphasized by a graph-type bar.

Nutrients per ¼ Pizza	
Calories	**240**
Sodium	**640mg**
Fat	7g
Protein	9g
Carbohydrates	35g
Percent of Daily Need:	
Vitamin A	15%
Vitamin C	8%
Calcium	10%
Iron	6%

Format A

Nutrients per ¼ Pizza	
Calories	**240**
Sodium	**640mg**
Fat	7g
Protein	9g
Carbohydrates	35g
	Rating:
Vitamin A	Good
Vitamin C	Fair
Calcium	Fair
Iron	Fair

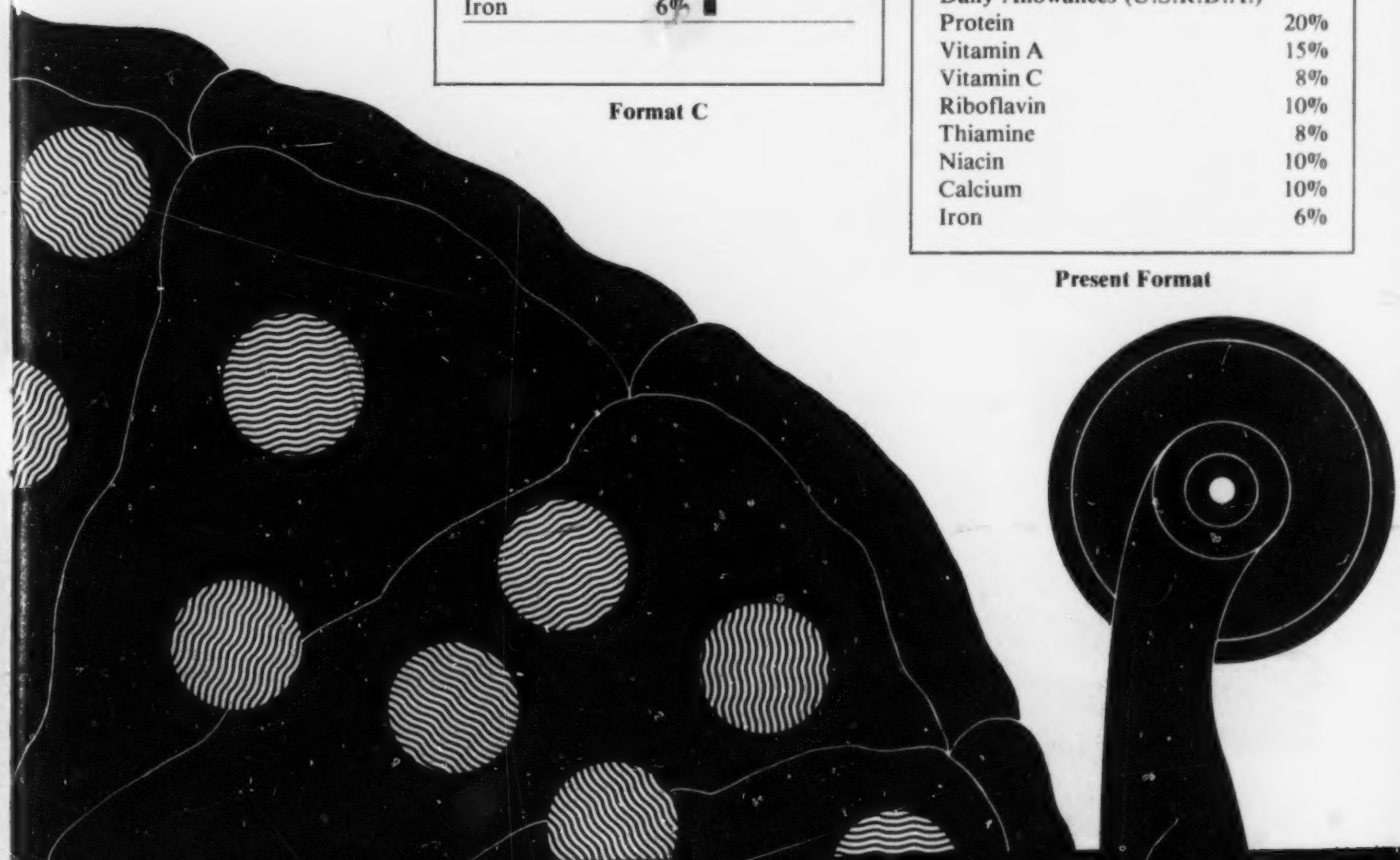
Format B

Nutrients per ¼ Pizza		
Calories		**240**
Sodium		**640mg**
Fat		7g
Protein		9g
Carbohydrates		35g
Percent of Daily Need:		
	0%	100%
Vitamin A	15% ■■	
Vitamin C	8% ■	
Calcium	10% ■	
Iron	6% ■	

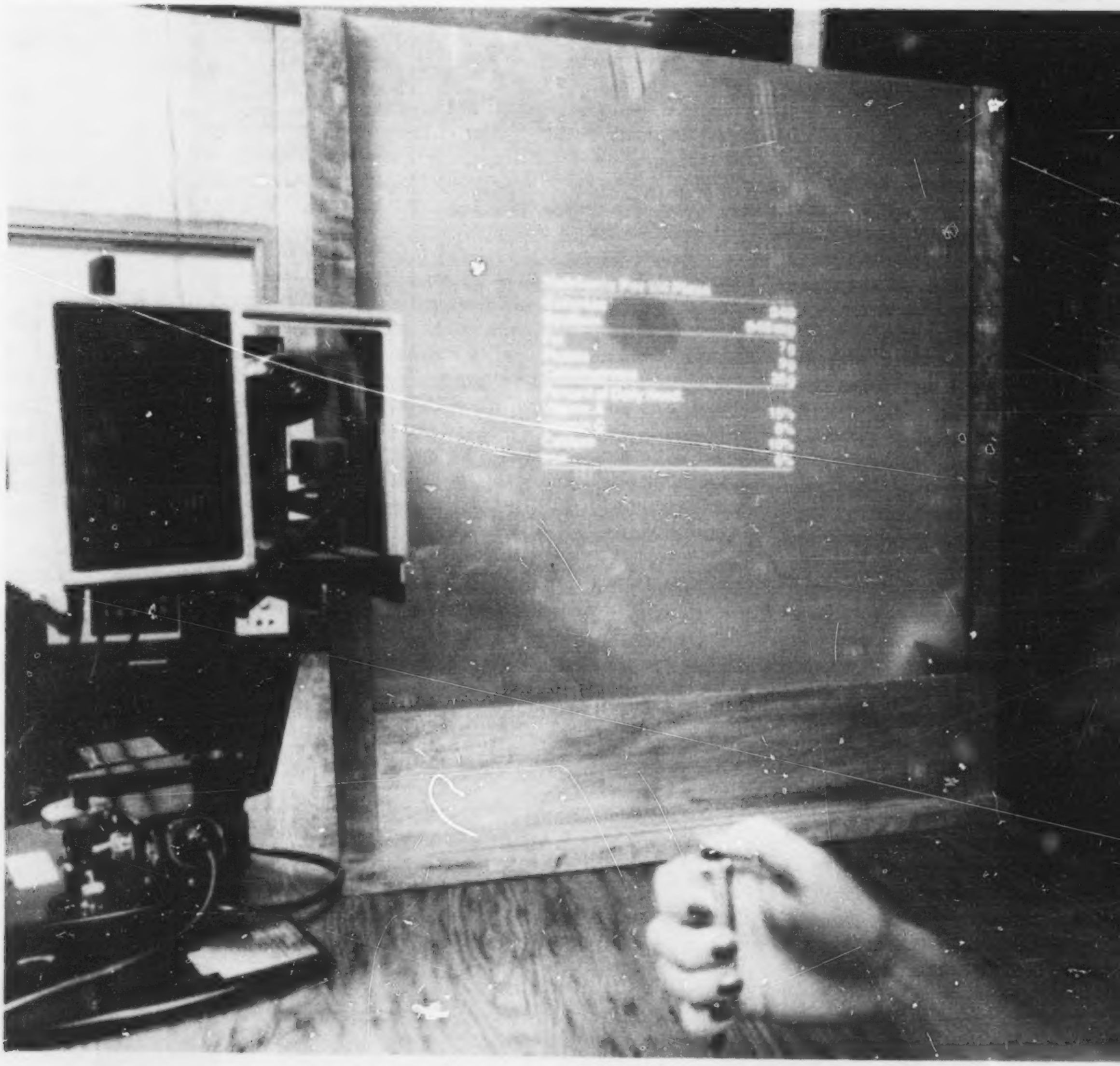
Format C

Nutrition Information Per Serving	
Serving Size	¼ Pizza
Servings Per Container	4
Calories	240
Protein	9g
Carbohydrates	35g
Fat	7g
Percentage of U.S. Recommended	
Daily Allowances (U.S.R.D.A.)	
Protein	20%
Vitamin A	15%
Vitamin C	8%
Riboflavin	10%
Thiamine	8%
Niacin	10%
Calcium	10%
Iron	6%

Present Format



Below, a woman reads nutrition label information shown on a viewing screen while an eye camera records her eye movements and reading patterns. The camera will record what she looks at (and doesn't look at), the sequence in which she reads the label, and how long she spends reading each part. After the eye test, the woman will be questioned to test her understanding, recall and reactions to the label format, one of several designed to improve nutrition labeling. On the other side of the eye camera a researcher, right, is monitoring the screen and equipment. It is this type of basic testing FDA hopes to use with approximately 800 people to determine which of its various nutrition label designs seems most useful to consumers.



uses of foods vary. Second, the amount of nutrients needed by individuals varies according to age, sex, size and even lifestyle. Third, food comes in all sizes of packages, and the amount of space on the label available for nutrition information will vary. Fourth, the public's understanding of nutrition is not what many nutritionists would like it to be.

When the Gersin firm began developing alternative labeling formats, it came up with several dozen design formats. Some modified the present label, while others incorporated bars, charts and other features. The number of formats to be consumer-tested will probably be boiled down to about a half dozen that are deemed the best candidates.

To understand the thinking that has gone into the alternative formats, some of which are illustrated with this article, an understanding of what is required on the present label is necessary. The present nutrition labeling was an outgrowth of recommendations made during the 1969 White House Conference on Food, Nutrition and Health. With the cooperation of the food industry, nutritionists and consumers, FDA in 1973 published the nutrition labeling requirements that are in effect today. The information now presented, the language used, even the order in which the nutrients are listed were outlined by the 1973 regulation. Currently, about 44 percent of packaged food sales in the United States involves products that have full nutrition labeling. About half of these sales deal with products for which such labeling is mandatory and the rest with products for which the manufacturer chose to use nutrition labeling.

Under the regulations, complete nutrition labeling is required only if a nutrient is added to a food or if a nutrition claim is made about the food. For example, if a product is described as high in vitamin C, low in sodium, low in calories, low in fats, or as a good source for any kind of nutrient, FDA considers these as nutritional claims and requires full nutrition information on the label. When a manufacturer does choose on his own to use nutrition labeling, he must follow the prescribed format. (See illustration accompanying this article of a current nutrition label.)

On most foods, ingredients also must be listed. The ingredient used in the largest amount by weight must be listed first, followed by others in descending order according to the amount used. However, the amount itself does not have to be stated.

The new labeling ideas focus mainly on the nutrition information sections of the label. The various formats prepared by the Gersin firm are based, for illustration, on information that would appear on the label of a cheese pizza with four servings. Some of the format changes that are suggested by the alternative designs are as follows:

- The present label could be simplified by using more easily understood terms and wording. For example, "Percentage of U.S. Recommended Daily Allowances (U.S. RDA)," was reworded to simply say, "Percent of Daily Need." Instead of two lines saying "Nutrition Information Per Serving" and "Serving Size," these terms are combined into one. In the case of the cheese pizza, it is expressed as "Nutrients Per ¼ Pizza."
- The amount of required information could be reduced, leaving manufacturers with the option of adding to it. Currently, thiamine, riboflavin and niacin must be listed in nutrition labeling. Many nutrition experts believe these vitamins are plentiful in the diets of most Americans because of vitamin and mineral enrichment of many products. Consequently, these three vitamins do not appear on various Gersin designs.
- The information now required in nutrition labeling is organized differently in various Gersin designs. The firm noted that the present format does not group information by category nor show the information in any sequence of priority. Likewise, no special emphasis is given to certain nutrition information—such as sodium content—that might be deemed important in a particular food product.

The label designs acknowledge the diet-related health concerns indicated by consumers in FDA surveys. Obesity or excess calorie consumption is the leading concern of most consumers; as a consequence, calories are at the top of the Gersin designs. Sodium, because of its association with hypertension (high blood pressure), is high on the list. Fat also appears higher because of public concern with this substance. Dark, boldface type and underlining also are used by the firm for emphasis.

Under present labeling requirements, it is difficult for a consumer to compare nutrients, the Gersin firm noted. There are different serving sizes for products; a figure for total servings also appears; calories, protein, carbohydrate and fat are identified in grams, a term many experts believe is not easily understood by consumers; and the recommended daily allowances appear as percentages.

One FDA survey showed that only 6 percent of the consumers who look for nutrition information actually read the entire nutrition portion of the label. This suggests that the consumer may be overloaded with information under the present format, or it could mean the consumer is seeking limited information. The forthcoming research will try to find out how much information is appropriate for food labels.

In trying out the different design formats, FDA plans to conduct testing with groups totaling 800 people. Included will be consumers who are 65 and older; those who have less than a high school degree; those who have diet-related health problems in their immediate families; and those who have at least a high school education and have no known diet-related health concerns in their family.

One of the key pieces of equipment to be used in the testing is an eye camera. FDA's Raymond Stokes believes that the best label design is one that permits a consumer to quickly find the information he or she needs, read it, comprehend it and use it. With the eye camera aimed at the subject, it is possible to measure with great precision what the eye is focusing on and the length of time the eye is fixed on a piece of information. This pinpoints what the consumer is actually interested in reading and how long he or she spends on it. It also will tell what the consumer is not reading and whether a consumer has to reread or double-check any label information.

After the eye camera tests are completed, interviews will reveal the test subjects' understanding of the formats; what caused confusion; what information was accepted with confidence, or rejected; whether diet and health-related information influenced the selection of food; and, generally, how satisfied the consumer was with the various labels.

Chris Lecos is a member of FDA's public affairs staff.

FDA's New Code: A Clean Sweep For Food Stores

by James Greene

Each day, millions of shoppers walk up and down the aisles of food supermarkets, grocery and convenience stores, making their purchases with assurance that what they are buying is safe to eat.

But few venture beyond the aisles to the areas where the food is received, stored and prepared for displaying. It is primarily in these areas that insanitary practices by employees are most likely to occur. Improper storage or handling of foods, particularly perishables, could result in foodborne illnesses such as salmonella for persons who eat the food.

Assuring that food in retail stores is handled in a safe and sanitary manner is the responsibility of the food industry and an army of sanitarians and inspectors who work for an estimated 3,500 state and local government agencies that regulate the more than 165,000 retail food stores throughout the country.

However, the sanitary standards established by the many regulatory agencies often vary considerably from each other, causing unnecessary confusion, complications and expense to food stores, especially to large chain stores that operate interstate or in multiple local jurisdictions, or both.

The need for a uniform set of standards across the nation is obvious. Working with the Association of Food and Drug Officials, the Food and Drug Administration has developed a proposed model retail food store sanitation code. It was based on a review of more than 30 existing state laws.

The code will function two ways. It provides sanitation guidelines that can be used by operators of retail food

stores to keep their establishments clean, and it sets uniform sanitation standards for these stores that can be adopted and enforced by local and state governments.

After review by state and local officials, the code was issued this summer by FDA. Once adopted by a state or local government agency, its inspectors can use the code for inspecting not only retail food stores but also such specialized retail operations as meat and fish markets, candy stores, bakeries, delicatessens and ethnic food stores.

State and local government agencies have the option of adopting the complete model code or whatever sections they think may improve their existing sanitation standards.

The code covers the complete sanitary operation of a retail food store, including storage, preparation and display; employee practices, equipment design and cleanliness; construction and maintenance of physical facilities; and storage and use of toxic substances.

Art Banks, director of the retail food protection branch in FDA's Bureau of Foods, expects extensive use of parts or all of the code by industry trade associations such as the Food Marketing Institute, Grocery Manufacturers Association, National Association of Retail Grocers, and the National Association of Convenience Stores.

The Food Marketing Institute is already incorporating the code into its training program. John Farquhar, FMI vice president of education and technology, called the model code "a very workable document."

Farquhar said that FMI, the largest single trade association of retail food stores in the country, is developing a comprehensive education program in cooperation with FDA to aid store managers in complying with the code.

Farquhar said FMI is developing a compliance manual and an audiovisual slide presentation to explain the code in detail, including inspection procedures and drawings of various types of sanitation violations.

Farquhar also said posters will be made available for placing in key points throughout stores to illustrate important basics, such as the temperatures required for storing frozen, refrigerated and hot foods. Small reminder cards will be distributed to employees on the same themes, Farquhar said. All these actions, Farquhar concluded, will help in the practical application of the model code.

For its enforcement, the model retail food store code offers compliance procedures for local officials. Some of these key elements include:

- Issuing permits to operate a retail food store: A retail food store would be inspected to determine that it is designed, constructed and equipped for proper operation before the operator can get a permit.
- Using a standard inspection report form: Sanitarians would use a 100-point inspection report to determine violations and assign their numerical importance. A sewage backup in the store, for example, would be assigned a 5-point penalty, the highest,while inadequate lighting in a store would be assigned a 1. If a firm received a total score of 59 or less it would have to take corrective actions within 48 hours.
- Establishing frequency of inspection: Retail food stores would be inspected at least once every six months. Results of the inspection, summarized on the inspection report form, would be given to the operator.
- Suspending or revoking permits based on violations: The suspension could occur immediately, without notice, if the sanitarian determined that the violations posed an imminent hazard to the public health. Serious or repeated violations could result in the revocation of a permit, provided the firm is given 10 days notice and the opportunity for a hearing.

Two agencies of the United Nations—the Food and Agriculture Organization and the World Health Organization—also have expressed interest in the model code. A committee of food experts established by these two agencies is charged with setting international food standards, including the safe and sanitary handling of food at the retail level.

The Model Retail Food Store Sanitation Code is the third and final code issued by FDA since 1976 to improve the sanitary handling and display of virtually all food sold at the retail level. In 1976 the agency issued a code designed specifically for restaurants, and in 1978 it issued a code aimed at food sold through vending machines.

James Greene is a member of FDA's public affairs staff.

THE THYROID

More Than A Pain In The Neck

by Annabel Hecht

Its name comes from a Greek word meaning shield, but in truth the human thyroid gland looks more like butterfly wings on either side of the windpipe. The thyroid is one of several small, powerful glands known as endocrine (or ductless) glands because they release their hormones directly into the bloodstream. (Other endocrine glands are the pituitary, parathyroid, adrenal and sex glands and the insulin-producing islets of Langerhans in the pancreas.)

The thyroid is probably the best known of the endocrines. Because of its location it can be felt easily with the fingers, and when something goes wrong it may become visible, even to the untrained eye.

From its command center at the base of the neck, the thyroid gland sends out two hormones that control the rate at which food is converted into heat and energy in all cells of the body. Thyroid hormones also affect growth and development, help regulate lipid (fat) metabolism, and increase the absorption of carbohydrates from the intestines. The manufacture and release of the thyroid hormones are controlled through a sensitive feedback system involving the hypothalamus and the pituitary gland, both located in the brain.

The system swings into action when levels of the thyroid hormones in the blood fall. First, the hypothalamus secretes a special hormone that stimulates the pituitary to secrete TSH (thyroid-stimulating hormone). Then, the TSH is transported to the thyroid gland where it turns on the hormone-producing mechanism. When thyroid hormone levels are adequate for the body's needs, the pituitary gland turns off the TSH release. Thyroid hormones reach their destination via the bloodstream, most of them bound to proteins in the blood. However, some remain in a free state.

Iodine is essential for the production of thyroid hormones. In fact, one of them, thyroxine, is 65 percent iodine by weight and the other, triiodothyronine, is 58 percent iodine. The thyroid is the only gland that requires iodine.

The main sources of iodine are food, water and medicine. Exactly where all of it comes from was discussed in "Iodine: Going From Hypo to Hyper" in the April 1981 *FDA Consumer*. Ingested iodine is absorbed through the intestines and carried to the thyroid gland via the blood. The gland can store this element for 10 weeks or longer. Despite this remarkable ability, the thyroid may sometimes over- or underproduce its hormones. When this happens over a period of time, serious health problems can result, including abnormal growth and mental development and even life-threatening heart disease.

The most familiar thyroid disease is goiter, usually the result of too little iodine in the diet. When the thyroid gland doesn't have enough iodine, it enlarges in an effort to capture all it can of that essential element from the blood. At the same time, the hypothalamus and pituitary gland are sending signals that more hormones are needed, forcing the thyroid to try harder. The enlarged gland is the swelling in the neck, once so familiar in some areas of the United States where the soil lacks iodine.

Goiter is an old health problem. Marco Polo (circa 1300) and Garcilasco de la Vega, a 16th century chronicler, observed cases of goiter during their travels. Before iodine was added to salt, beginning in 1924, goiters were common in Central Europe and the Great Lakes region in the United States. The disease still afflicts 200 million people worldwide, mostly in underdeveloped and mountainous areas.

Women are more likely to develop goiters than men. In areas where there is a severe iodine deficiency, most adolescent children are affected. Lack of iodine is not the only cause of goiter. Hormone production can be blocked by certain drugs, including the sulfonylureas, used in the treatment of diabetes, and lithium, used in the treatment of psychiatric disorders.

Large amounts of iodine also can interfere with hormone production. Some foods, such as rutabagas, cabbage and turnips, contain a substance that can be converted to an active anti-thyroid agent called goitrin. The amount of goitrin people get in a normal diet is not enough to be harmful, but among vegetarians "cabbage goiters" do occur.

Simple goiter in its early stages can be treated with iodine as well as with natural or synthetic thyroid hormones. Large goiters sometimes are removed surgically to improve the patient's appearance and to relieve pressure on the windpipe. When this is done, the patient must take thyroid hormone preparations to prevent regrowth of the goiter.

The same conditions that cause simple goiter also can lead to nodules in the thyroid. It is difficult to determine whether such nodules are harmless or cancerous without the skills of a thyroid specialist. Most thyroid cancers are slow growing, however, and thus are likely to be discovered in time for successful treatment.

Any condition in which the thyroid gland produces an excess of hormones is called hyperthyroidism, or thyrotoxicosis. One of the most common forms of this condition is Graves' disease. The symptoms of this disease include excessive sweating, often accompanied by an intolerance for heat, plus palpitations of the heart, nervousness and irritability, hand tremors, and weight loss despite a good appetite. Protruding eyes give the patient a staring expression. This is aggravated by lid lag—that is, the eyelid does not follow the eyeball when the gaze is turned downward, leaving the white of the eye exposed. The eyelids may also be puffy.

Sudden severe flare-ups of the disease sometimes occur, often following an infection, trauma or surgery. Called thyroid storms, such episodes can be fatal. However, this phenomenon is rare.

The exact reason for the hormone overproduction of Graves' disease is unknown. However, the disease appears to run in families; it affects women more often than men, and it seems to develop after a severe emotional upset. Graves' disease can be treated by blocking hormone production with anti-thyroid drugs such as propylthiouracil or methimazole or by reducing gland size and function with radioactive iodine. Surgery to remove part of the gland, leaving enough to keep it functioning normally, is used much less frequently now than in the past.

About a third of the patients treated with drugs can discontinue treatment in a year, but the remainder may need to take thyroid medication the rest of their lives. Patients with Graves' disease should have periodic check-ups since any one of these treatments can cause the thyroid gland to become underactive.

An underactive gland—one that is not producing enough hormones—leads to the condition called hypothyroidism. The gland may fail to do its job because of diseases affecting the hypothalamus and pituitary gland, destruction of thyroid tissue by inflammation or excessive treatment of hyperthyroidism, or lack of iodine.

Hypothyroidism can appear at any age. Infants can come into the world with it if their mothers didn't get enough iodine or were treated with radioactive iodine during pregnancy. In newborns the condition is called cretinism. The symptoms usually appear during the first month or two of life. The infant is listless, eats poorly and is constipated. The skin is pale or has a dusky, mottled appearance, the face is puffy and the tongue broad and thick. Unless the infant is treated promptly, its physical and mental growth will be retarded.

Hypothyroidism beginning in early childhood is called juvenile hypothyroidism. In this condition the development of mental retardation is not as severe as that of cretinism. Physical growth and sexual development are predominantly affected. Juvenile hypothyroidism may result from hypothalmic or pituitary disease or a defect in iodine metabolism.

The classic symptoms of hypothyroidism in adults include a sensitivity to cold, skin that is dry and sometimes thickened, puffy eyes, increased weight, coarse and brittle hair, and fatigue and sleepiness. In its severe form, this condition is called myxedema.

Often an adult with hypothyroidism may have only mild or isolated symptoms and the disease may come on so gradually that even close friends are not aware of a change. Often, too, mild symptoms of adult hypothyroidism are mistaken for something else, such as depression.

Fortunately, juvenile and adult hypothyroidism are easy to treat. The patient need only take synthetic or natural sources of thyroid hormone. Infants whose cretinism got its start before they were born can be saved from mental retardation if they are treated with hormones before they are 3 months old. According to experts in this field, four-fifths of children with congenital hypothyroidism who are diagnosed and treated early will have IQs above 90. The best form of treatment, however, is prevention—that is, making sure the expectant mother gets enough iodine in her diet.

Another group of thyroid disorders goes under the general heading of thyroiditis. Acute thyroiditis is a rare result of a bacterial infection. The symptoms are those of an inflammation: heat, pain, redness and swelling. The treatment is the same as that used in any illness accompanied by fever. To combat the bacterial infection, antibiotics are used.

Subacute thyroiditis is a more common illness that produces a swollen and tender thyroid gland along with a fever. Usually the cause is unknown, but the disease is sometimes associated with the virus that causes mumps. Aspirin or other pain relievers and thyroid hormones are used as treatments for the disease.

Another disease, chronic thyroiditis, comes in two varieties. One is Hashimoto's disease, a chronic disorder involving a painless enlargement of the thyroid gland. Once thought a rarity, it is now recognized as one of the most common of the thyroid disorders. It is thought to be an autoimmune disease—that is, the victim seems to be allergic to herself (women are 20 times more likely than men to develop this condition). If the goiter is small, treatment may not be necessary. However, under some circumstances thyroid hormones may be prescribed.

In the second chronic condition, Reidel's thyroiditis, the gland is replaced by a mass of dense fibrotic tissue. The cause of this rare condition is unknown, and the only treatment is surgical removal of part of the gland to relieve pressure.

In some cases of thyroid disease the patient's appearance is a clue to the diagnosis. The swelling of the neck in goiter or the "pop eyes" of Graves' disease are dead giveaways. But the symptoms of a thyroid problem are not always so obvious. Fortunately, sensitive laboratory tests are available to aid in the diagnosis of thyroid conditions. These include measurements of the amounts of thyroid hormones in the blood or the level and activity of the pituitary thyroid stimulating hormones.

Radioactive iodine is another diagnostic tool used to study thyroid function and structure. Given to the patient either in capsule form or dissolved in water, the radioactive iodine homes in on the thyroid gland. By measuring the amount of radiation emitted by the gland, using a detector positioned outside the patient's neck, the doctor can obtain an image of the gland and can determine whether it has absorbed iodine as it should. The radioactive isotope of iodine traditionally used in this procedure has been iodine 131 (^{131}I). A newer form of radioiodine, ^{123}I, can do the same diagnostic job with less radiation exposure to the patient.

It is estimated that one in 5,000 newborn infants in North America has hypothyroidism which, if not promptly treated, will result in permanent mental retardation. This suggests that infant hypothyroidism may be one of the most common treatable causes of mental retardation. Screening tests for this form of hypothyroidism have been developed and are being used in some countries and in some states in the United States. The American Academy of Pediatrics recently recommended that such screening programs be available for all infants.

Annabel Hecht is a member of FDA's public affairs staff.

Potassium Iodide... What To Do About It

FDA has issued its final recommendations on the use of potassium iodide to help protect the public from thyroid injury during a radiation emergency. Such an emergency might occur as a result of an accident at a nuclear power reactor where large quantities of radionuclides, including isotopes of radioiodine might be released into the atmosphere.

When radioiodines are inhaled or ingested, they rapidly accumulate in the thyroid gland and are metabolized into organic iodine compounds. These compounds could reside in the thyroid gland long enough to cause local radiation damage, such as thyroid nodules or cancer.

Potassium iodide helps prevent such injury by saturating the thyroid gland with non-radioactive iodine. This blocks the thyroid from absorbing the radioactive iodine from the air or contaminated water, milk or foods. The radioactive iodine is instead excreted from the body.

Potassium iodide is a component of the normal diet; it is added to salt as a goiter preventive; it is available in a variety of non-prescription products, particularly salt substitutes and certain vitamin products; and it is used in prescription products for treatment of respiratory diseases. Potassium iodide as a thyroid-blocking agent for use in a radiation emergency is now commercially available in both tablet and solution form.

FDA says that state and local public health officials should consider use of potassium iodide in radiation emergencies by people who are likely to receive a radiation dose of 25 rems, or greater, from radioactive isotopes of iodine released into the environment. (A rem is a unit of measure of radiation exposure in people.) This exposure level is consistent with other radiation protection guidelines from the U.S. Environmental Protection Agency and guidelines used in the United Kingdom.

The dose of potassium iodide recommended by FDA is 130 milligrams per day for adults and children more than 1 year old and 65 milligrams per day for children less than 1 year old. These doses can block about 90 percent of radioiodine absorption if the first dose is given a few hours before or immediately after intake of radioiodine. Even if the first dose is given three or four hours after exposure, the drug can still block about 50 percent of radioiodine absorption.

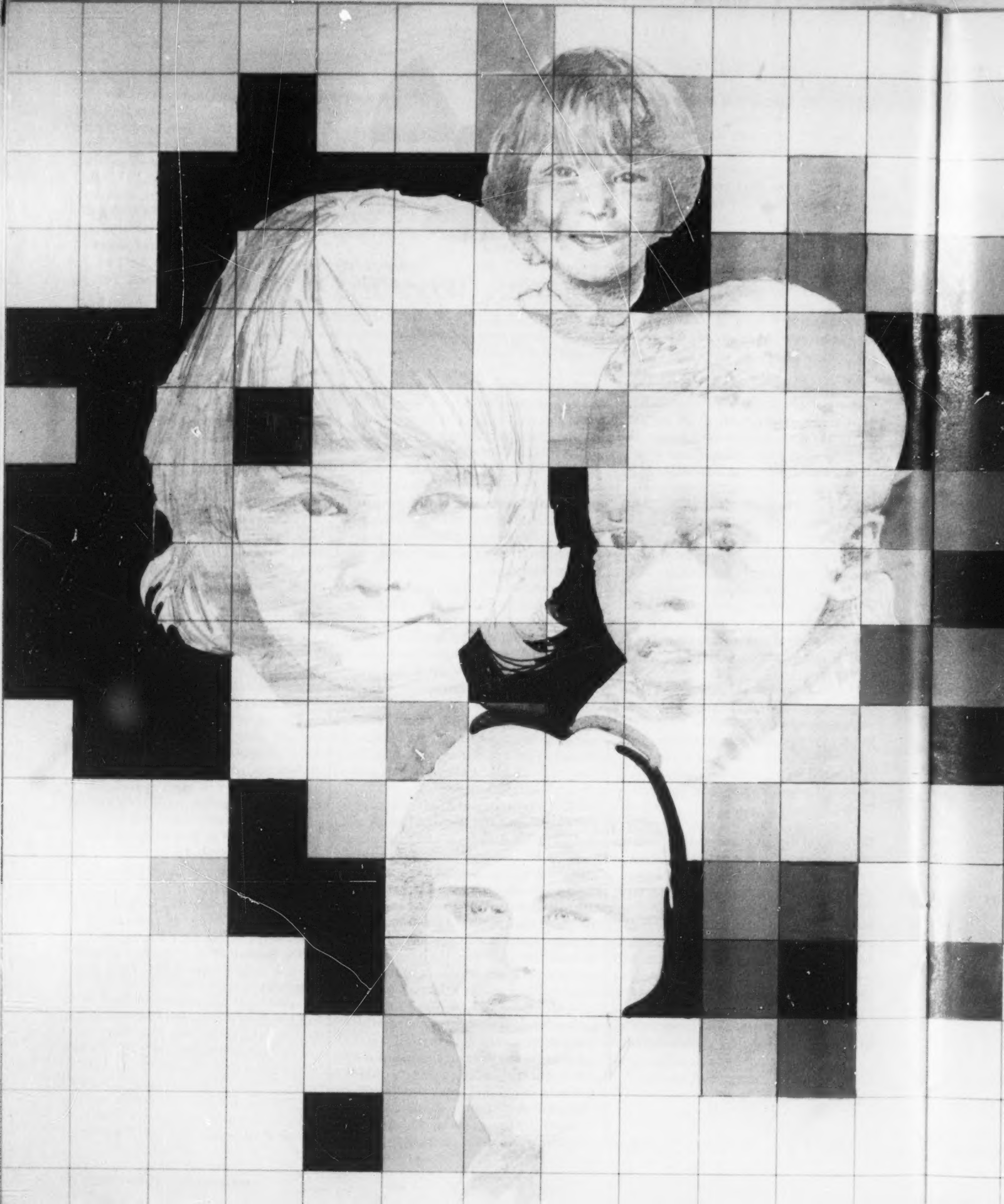
FDA's recommendations also urge state and local officials who decide to include potassium iodide in their plans to establish a system for informing the public on how to use the drug, how to report side effects, and how to get treatment for any adverse reactions. Because it is important that the public be given specific information on its safe and effective use, the drug is available only to nuclear facilities and state and local authorities.

It is not known how many significant adverse reactions would result from short-term use of thyroid blockers in the doses recommended by FDA, but it is expected there would not be many. The agency concluded that the risks from the short-term use of relatively low doses of potassium iodide in a radiation emergency are outweighed by the risks of radioiodine-induced thyroid nodules or cancer at projected doses of 25 rems.

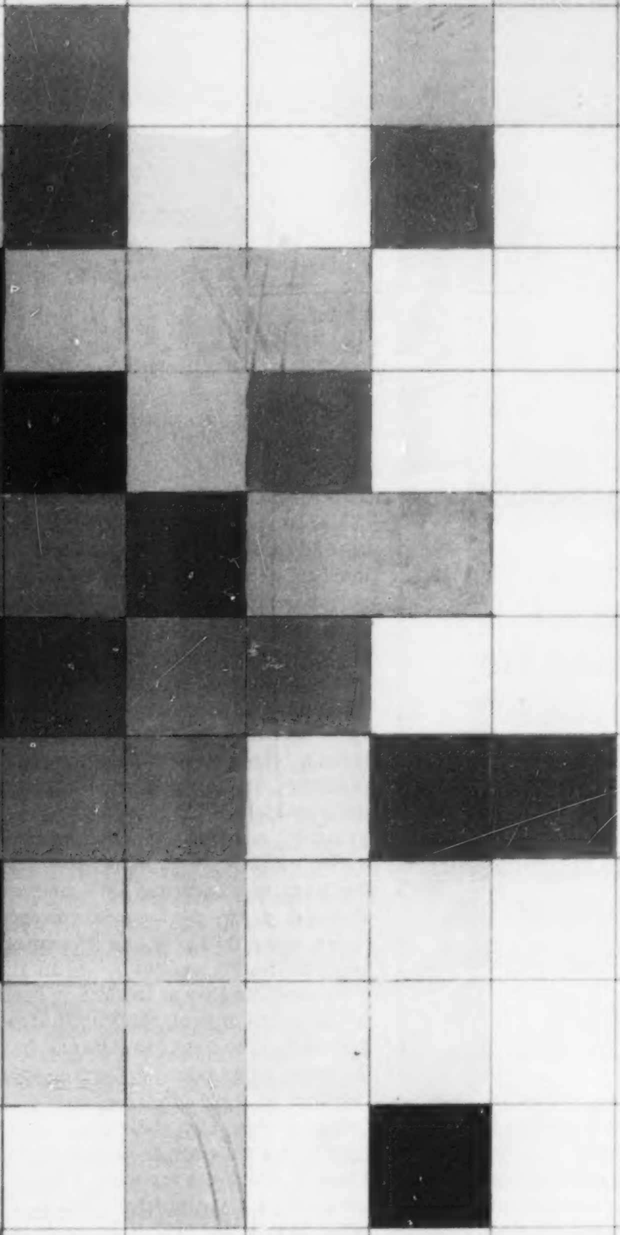
FDA's recommendations will be included in radiation emergency guidelines being prepared by the Federal Emergency Management Agency for use by state and local officials who may decide to distribute potassium iodide as part of their emergency response plans. The recommendations are not binding; the decision as to when and how to use the drug, if at all, remains with state and local officials. (Last fall, the Tennessee Department of Public Health distributed potassium iodide tablets to about 7,000 families living within five miles of the Sequoyah nuclear plant near Chattanooga.)

The use of potassium iodide in a radiation emergency is not a panacea, FDA stresses in its recommendations. It does not reduce the uptake or storage by the body of other radioactive materials or provide protection against external radiation. Other protective measures, such as providing shelter and respiratory protection and evacuating affected persons, also need to be considered, the agency says.

The recommendations on use of potassium iodide can be obtained from Bernard Schleien, Pharm. D., FDA, Bureau of Radiological Health, HFX-4, 5600 Fishers Lane, Rockville, Md. 20857.



Reye Syndrome Spells Caution To Parents



by Richard C. Thompson

Reye syndrome (pronounced "rye" and sometimes called RS or Reye's syndrome) is an acute condition that may follow influenza or chicken pox infections in children from 1 month to late teens. It is characterized by persistent vomiting, violent headaches and bizarre mental and physical behavior in children who appear to be recovering from an often mild viral illness. It requires immediate diagnosis and admission to a hospital where emergency care can quickly be provided. Although a rare complication of common viral infections, when it does occur Reye syndrome is considered life threatening.

Until 1963, what is known as Reye syndrome did not even have a name. In that year, an Australian pathologist, Ralph Douglas Reye, described the course of the illness and the pathology findings from 22 children whose influenza illness had been followed by the same syndrome. This description went into the medical literature under Reye's name.

But even though it now had a name, RS still went largely unrecognized by physicians and the public. For one thing, being in the medical literature did not mean that RS immediately became well known. It takes time, often years, for cases to accumulate and be reported, for medical scientists to learn of new findings through journals and professional meetings, for physicians and researchers to share their experiences. This is true of all medical knowledge; it was true of RS. It was well into the 1970s before Reye syndrome was readily recognized and diagnosed.

The nature of influenza in children

does not make a diagnosis of RS easy. Flu is considered a minor illness, often treated at home with aspirin or other medication and seldom needing the attention of a physician.

When Reye syndrome occurs, it is considered life threatening.

Reye syndrome seems to occur where influenza strains A and B are prevalent.

If the illness developed into and was recognized as Reye syndrome, the child would likely be taken to a hospital where "aggressive" treatment could be done. This could include skull surgery to relieve pressure on the swollen brain and, in some cases, repeated whole blood exchange transfusions and kidney dialysis, to help cleanse the body of toxic accumulations. It could also include intravenous fluids, respirators and very close monitoring of the patient so that if the condition worsened other measures could be used.

These methods for treating RS patients were developed in the 1960s and early '70s. Unfortunately, most of the children diagnosed and treated in this time period were severely ill and deeply comatose when admitted to the hospital, and their chances for survival were poor.

The death rate for Reye syndrome patients was nearly 80 percent until just a few years ago. Today it is 20 to 30 percent. One reason for the still high mortality rate is that Reye syndrome simply overwhelms a patient, and can do so in a matter of hours. By the time the parents realize that the child recovering from a viral illness has suddenly become very ill, there may be little time left. There are many tragic stories of a child coming out of influenza, then beginning to vomit, then becoming lethargic, then violent, and finally slipping into a coma—all within less than a day.

Few parents can respond to the swift, frightening sequence of events that may develop from a simple case of the flu. One of the more tragic deaths was that of the 11-year-old son of a Washington, D.C., physician who, even as he was rushing the boy to the hospital, realized that it was too late. The father, with other parents who have lost children to Reye syndrome, helped establish the National Reye's Syndrome Foundation to sponsor research into the illness and to educate the public about the syndrome. The research program is based at Ohio State University in Columbus.

The foundation has several goals beyond public education and research. It wants Reye syndrome to be a reportable disease, meaning that physicians must formally report to state health officials on cases they have treated. It wants Reye syndrome emphasized in teaching hospitals and schools of medicine, family physicians trained to quickly recognize and diagnose the condition, and hospital emergency staffs instructed in the aggressive treatment needed for the RS patient. It also wants a simple diagnostic test that can quickly identify RS, and a set of therapies that all hospital emergency teams would know and immediately apply to the RS patient.

Epidemiologists at the U.S. Centers for Disease Control, the Public Health Service facility based in Atlanta, have for many years been conducting surveillance of Reye syndrome in the United States. They estimate a total of 1,200 cases nationwide each year, only a few of which are reported. During the reporting period from Dec. 1, 1980, to Oct. 31, 1981, CDC received written reports of 221 cases of defined Reye syndrome from 39 states and the District of Columbia. Where age was reported, 73 were 4 years old or under; 124 were 5 to 14; and 12 were 15 and older. Where sex was reported, half were male, half were female. There were 58 fatalities in the 208 cases for which outcome of the illness was reported (outcome was unreported in 13 cases). This ratio of deaths to total cases (under 30 percent) has changed

little in the past three years.

Reye syndrome is known to occur throughout the world, but it is poorly recognized and diagnosed in most countries, and reported to public health authorities in almost none. One problem is that Reye syndrome can resemble the symptoms of other illnesses, such as meningitis, encephalitis, or even drug overdose hallucinations. This makes the syndrome easy to misdiagnose.

Dr. Robert Dobrin of Children's Hospital in Denver, experienced in pediatric emergencies, lists several tests that the clinician should order to make a Reye syndrome diagnosis. They include blood sugar, serum glutamic levels, and a toxicology screening.

Dobrin and others describe five stages seen in RS patients: stage I: vomiting, lethargic, responsive to commands; stage II: disoriented, delirious but responsive to stimuli; stage III: comatose, some body rigidity, unresponsive to stimuli, failing respiration; stage IV: deepening coma, decerebrate (loss of brain function) rigidity, fixed pupils; stage V: cardiovascular failure, fixed and dilated pupils, respiratory failure and arrest.

More than half the cases reviewed in a 1977 study (following an earlier influenza B epidemic) went through at least two stages, with the chances for survival dropping rapidly during and after stage III. The deeper the coma and the younger the patient, the less the chance for survival. Through early diagnosis and quick, effective treatment, physicians strive to keep the patient in stage I or II.

One reason for the high mortality is that RS overwhelms the patient.

Aspirin and other salicylates may be associated with Reye syndrome.

The British medical journal *Lancet* pointed out in its April 24, 1982, issue that Reye syndrome appears to occur mainly in those places and at those times that influenza strains A and B are prevalent. RS also occurs, said *Lancet,* as single cases throughout the year, often associated with chicken pox (varicella) and certain other viral infections. RS related to chicken pox is seen mostly in children 5 to 9, and RS related to influenza B in children 10 to 14. Although RS has been reported in 4-day-old infants and in adults, it appears most often in children from 6 months to 15 years.

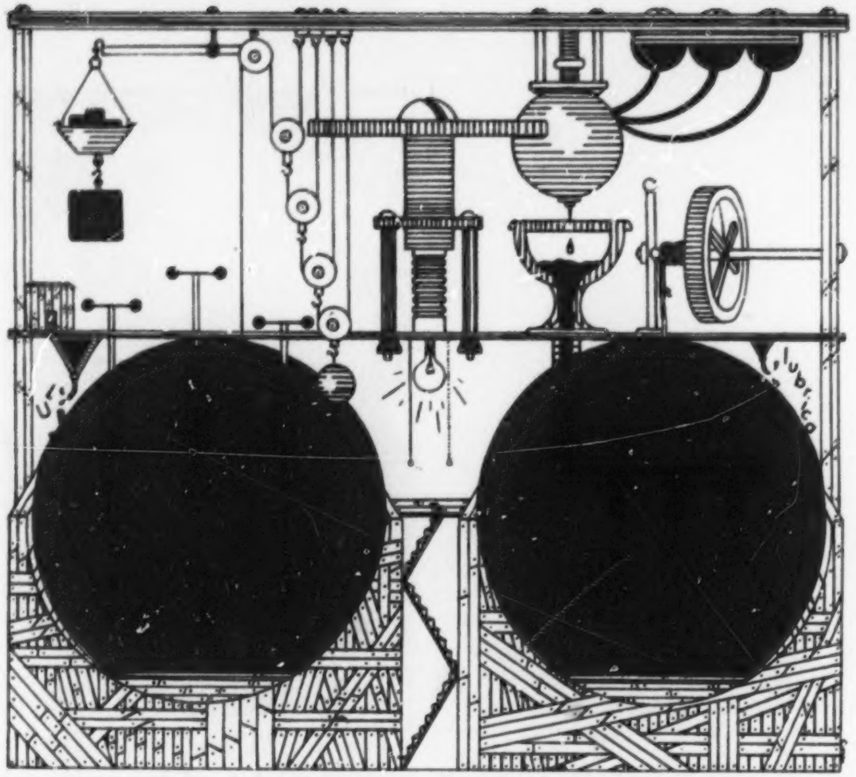
While the mortality rate for RS has dropped dramatically, as more has been learned about its signs and symptoms and the need for prompt diagnosis and treatment, the cause still remains unknown. Until more research returns are in, knowledge about RS must be considered preliminary.

One point, which has been supported by several studies in the past five years, is that aspirin and other salicylates may be associated with Reye syndrome. An Ohio review of RS cases during 1978-1980 found that 94 out of 97 children who had developed Reye syndrome had been given aspirin or other salicylate drugs, for the flu or chicken pox. Among a control group of children who had flu or chicken pox but who did not develop RS, only 110 of 156 had received salicylate drugs. These findings were consistent with similar reviews of Reye syndrome cases in Michigan and Arizona.

This pattern prompted the surgeon general of the Public Health Service to issue an advisory on June 11, 1982, cautioning against the use of salicylates and salicylate-containing medications for children with influenza or chicken pox. The American Academy of Pediatrics that same month advised parents and physicians against using aspirin (and other medicines) to treat the minor symptoms and fever of influenza and similar illnesses, basing its recommendations on those same studies.

Richard C. Thompson is a member of FDA's public affairs staff.

Excipients Give Drugs Versatility



The Ajax Pharmaceutical Corp. produces the antibiotic tetracycline. So does the Acme Drug Co. But that doesn't guarantee that the products are identical twins. There are any number of reasons why the products may not be the same. But the customer-patient has every right to expect that the tetracycline the doctor ordered will do the job that it is supposed to.

Seeing that Ajax's tetracycline has the same effect as Acme's is the job of the Food and Drug Administration. And the agency has set up regulations to assure that the same medicines from different manufacturers will behave the same way in the body and thus can be interchanged. (Ajax and Acme are fictitious firms, but there are four firms that make the antibiotic in capsule form and another five that make it in syrup form, according to the *Physicians' Desk Reference.)*

There's more to drugs than active (or therapeutic) ingredients. There are fillers, binders, lubricants, disintegrants, flavorings, coloring agents and diluents. All of those are inert ingredients that are classed as excipients. *(Dorland's Illustrated Medical Dictionary* describes an excipient as "any more or less inert substance added to a prescription in order to confer a suitable consistency or form to the drug; a vehicle.")

Sometimes these excipients can get in the way and affect how much of the active ingredient gets to its intended destination and how fast it gets there. This can make a difference between apparently similar drugs.

When a drug comes in a solid dosage form, such as a tablet, the excipients include binders, fillers, disintegrants and lubricants. In liquid forms, the excipients include flavorings and, of course, liquids.

Binders, such as ethylcellulose and liquid glucose, hold the therapeutic ingredients together. Too much binder can adversely affect the rate at which the drug dissolves in the body, while too little can result in tablets that crumble or otherwise deteriorate.

Filler is added to a dosage form to give it enough body to make it practical to handle. Some compounds contain only a small amount of certain potent drugs; therefore, there is more filler than therapeutic ingredient. If the filler binds (sticks) to the drug, bioavailability may be affected. (Bioavailability refers to the rate and extent of absorption of a drug's active ingredients in the body.) Starch is used as a filler, binder and disintegrant.

Disintegrants make tablets dissolve in liquid. If too much is added, a tablet may disintegrate in the bottle due to atmospheric moisture. If there is too little, the tablet may not disintegrate or break down in the body completely. This can affect the rate and amount of active ingredient that is released. Lubricants are important to the manufacturing process. They speed the flow of powder to the tablet manufacturing machine and they also prevent the tablet from sticking in the machine after it is compressed. Among the lubricants are stearic acid and magnesium or calcium stearate. These are hydrophobic materials; that is, they shed water or tend not to combine with it. Too little lubricant inhibits the manufacture of a satisfactory tablet while too much can make the tablet impervious to water and thus inhibit the disintegration of the tablet and the dissolution of the drug.

Capsules also contain fillers or diluents, disintegrants and lubricants. Chemical binders are unnecessary because the product is held together by its gelatin case. Flavoring and coloring agents have purposes, too. Flavoring can make liquid medicines and chewable tablets more palatable. Color also serves as a means of identification.

It is important to ensure that drugs which are supposed to be the same—such as the various brands of tetracycline—are the same, because in most states it is legal for pharmacists to substitute one drug for another similar product. In some states, substitution of a less expensive generic product is required of the pharmacist if the prescribing physician authorizes it. In some other states, the pharmacist can exercise discretion as to whether or not the substitution should be made even if the physician has indicated that substitution would be permissible. To help in making these decisions, FDA has prepared a list of all approved drugs, identifying those that can be safely interchanged.

The Notebook

The Notebook: a potpourri of items of interest gathered from FDA news releases, other news sources and the Federal Register *(designated* FR, *with date of publication). The* Federal Register *is available in many large public libraries.*

■ **John C. Villforth** has been named director of FDA's Bureau of Medical Devices. Director of the Bureau of Radiological Health since 1969, he will continue to hold this post. A merger of the two bureaus is planned as part of a series of steps undertaken by FDA to streamline and improve management of the agency.

■ Odette De Paris, a cosmetic distributor and beauty salon in Tarzana, Calif., has recalled tubes of **Refecto Cil permanent cream eyelash and eyebrow dyes** because they contain illegal coal-tar ingredients that may cause permanent injury to the eyes, including blindness. About 1,140 tubes of dye were distributed, primarily in California with some going to Pennsylvania and Michigan. FDA also issued an import alert to its field offices to prevent further importation of the dyes, which are manufactured by Gschwentner-Haarkosmetik, Vienna, Austria.

■ CHANGES IN BIOLOGICS REGULATIONS: FDA's biologics regulations have been amended to establish a 10-year dating period for **source plasma (human)** and to require an expiration date on product labels. Source plasma (human) is the fluid portion of human blood collected by plasmapheresis and is used as source material for further manufacturing into injectable and non-injectable products. Until now there has been no specific dating period, and manufacturing records have had to be kept indefinitely (*FR* July 16). . . . FDA is proposing to inspect **licensed biological establishments** at least once every two years instead of once every year, as is now required by law. The change will make the frequency of inspection of biologics manufacturers consistent with that of drug and device manufacturers (*FR* July 30).

■ A law banning **methaqualone** became effective July 1 in Florida. Similar legislation is pending in Alabama, Delaware, Louisiana and South Carolina.

■ Wrappers on individual sticks of **oleomargarine** or margarine no longer need to be labeled with the manufacturer's name and place of business. A new FDA ruling, effective July 27, also applies to unit containers of other foods in multi-unit and multicomponent retail food packages when the retail package and inner units are otherwise properly labeled and the inner units are not sold individually (*FR* July 27).

■ FDA is proposing to drop the publishing of its own list of **official names of drugs** in the *Code of Federal Regulations*. Non-proprietary drug names adopted by the U.S. Adopted Name (USAN) Council would then serve as "established names" of drugs, unless the agency finds the adopted name unduly complex or not useful. The agency has selected its official names almost entirely from those adopted by the council. The USAN Council was established in 1965 by the American Medical Association, the U.S. Pharmacopeial Convention and the American Pharmaceutical Association to provide a systematic method for assigning scientifically acceptable names to prescription drugs. FDA has been represented on the council since 1967 (*FR* July 16).

■ The amount of **aflatoxins** FDA allows in cottonseed meal used in non-dairy animal feeds has been raised from 20 to 300 parts per billion. Scientific information indicates the higher levels will not hurt the animals nor result in harmful residues in meat and eggs. Aflatoxins are byproducts of common, naturally occurring mold growth on certain foods and feeds. Some aflatoxins have been shown to cause cancer in test animals and in larger amounts are acutely toxic. Because they can't be totally avoided, FDA limits aflatoxins in food products sufficiently to protect the public health while assuring continued availability of those foods and feedstuffs that are susceptible to contamination. The current action was prompted by a request from Arizona where 76,730 tons of cottonseed meal remaining from the 1981 cotton crop was found to be contaminated with aflatoxins in excess of 20 parts per billion. If the meal could not be marketed it would have major adverse economic consequences in that state, the cottonseed oil mills of Arizona and California, and the cotton industry, according to representations made to FDA.

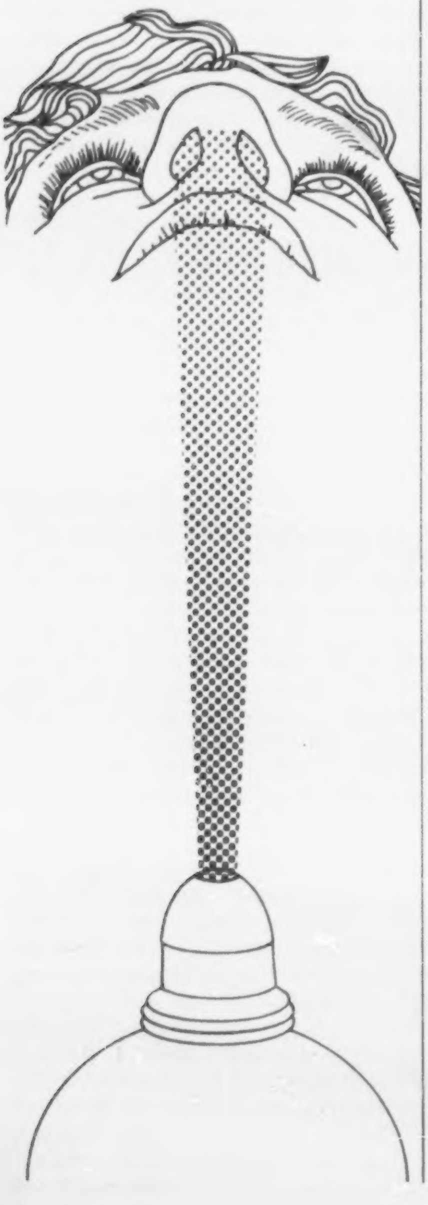
■ Latest additions to the **GRAS (generally recognized as safe) list** of direct human food ingredients are ammonium alginate, calcium alginate, potassium alginate, sodium alginate and propylene glycol. These substances are used as emulsifiers, stabilizers or thickeners in such foods as confections, frostings, gelatins, puddings, jams and jellies. Also considered GRAS are corn silk and corn silk extract (flavoring agents in baked goods, beverages, soft candy and frozen desserts) and sulfamic acid (an indirect food ingredient used in food packaging) (*FR* July 9).

Investigators' Reports

The Nose Knows

by Louise Fenner

An unusual sequence of quality control system failures at a manufacturing plant resulted in the production of 21,600 bottles of mislabeled nasal spray. The front side correctly carried the name of one type of nasal spray, but the back carried directions for another type. The mix-up escaped notice for three months before an alert consumer spotted it and notified FDA.



The labeling problem began four days before Christmas 1981. At the Bristol-Myers plant in Ladue, Mo., labels were being printed directly onto the front and back panels of plastic bottles intended for "4-Way Long-Lasting Nasal Spray." What went on the front of the bottles was the correct information. But on the back were printed directions for another product, "4-Way Mentholated Nasal Spray."

These non-prescription products are quite different. The long-lasting spray is not recommended for children except under a doctor's supervision and should be used by adults only once every eight to 10 hours. However, the incorrect labels stated that both children and adults could use the spray once every three hours.

Actually, a plant employee noticed the mistake after 21,600 bottles were mislabeled, notified the quality control department, and promised to destroy the bottles. The bottles were sent to a quarantine area to await destruction but were never destroyed. Meanwhile, the printing department changed the label on the back and printed 10,080 additional bottles correctly. These joined the mislabeled units in quarantine, where, according to company practice, all newly labeled bottles were kept until they could be examined.

The employees then took a Christmas break.

In January, the quality control department apparently assumed that the mislabeled bottles had been destroyed and permitted all the bottles in quarantine to be sent to a storage area. Following another examination, all the bottles were okayed and sent to the production area for filling. But the employees had relied on the labeling of the cases instead of looking at the containers themselves.

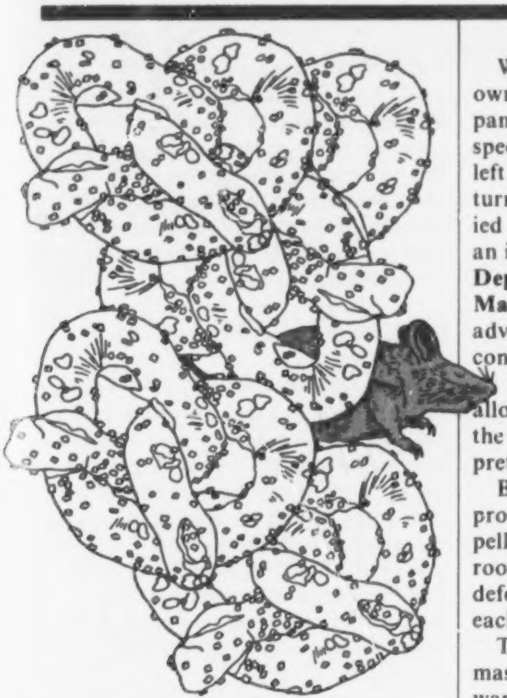
The bottles went past several more checkpoints during production. Labels were not checked at the beginning of the run as required. Following routine practice, employees reproduced the label of one bottle and attached it to the production record; it was a mislabeled bottle but no one caught it. Four reserve samples also were pulled out and saved for future reference in case of a complaint about the product. Since reserve samples aren't routinely examined for labeling, no one noticed that three of the four samples were mislabeled. At the end of the production run a sample carton of bottles should have been opened and carefully examined but wasn't. Instead, a single bottle was checked, and it happened to be correctly labeled.

Both correctly labeled and mislabeled bottles eventually reached retail stores. In April 1982, on a Friday, a consumer in North Carolina called FDA's Raleigh, N.C., resident post and pointed out the discrepancy between the front and back panels on a purchased bottle. FDA traced the bottle to Bristol-Myers' Missouri plant, and the following Wednesday sent out an investigator from St. Louis. By the next day Bristol-Myers began recalling 90,900 bottles, representing two production lots, to be certain that all the mislabeled units were accounted for.

FDA classified the recall as Class II because the incorrect labeling contained directions that would result in overdosing of children and adults. This recall classification covers situations involving possible adverse temporary or medically reversible health effects, but with serious injury unlikely.

The company subsequently informed FDA it had revised its quality control procedures to prevent a recurrence of the double labeling or similar problems.

Louise Fenner is a member of FDA's public affairs staff.



Open and Shut Case?

"Some circumstantial evidence is very strong, as when you find a trout in the milk," said Henry David Thoreau in 1854. That's how it seemed in Buffalo last December when a resident opened a bag of pretzels and found a dead mouse inside.

FDA's **Buffalo district** office confirmed the mouse was there, but noted there were no holes or teeth marks on the bag to show how the mouse got inside. Did it happen before the bag was closed, at the factory in Easton, Pa.?

The **Philadelphia district** office was notified and inspected the pretzel plant in Easton—Keystone Food Products Inc. But FDA investigators found no signs of rodents there, and the mystery widened.

Buffalo investigators then visited the grocery store where the pretzels were bought. The store too was free of rodents, but many bags of pretzels on the shelves had holes and teeth marks indicating rodent activity.

Then FDA went to the distributor's warehouse in Buffalo where the goods had been stored and walked into a scene of filth and contamination. The smell of rodent urine permeated all four rooms. One room housed tobacco. Candy and pretzels were stored in the other three. Rodent-gnawed bags of pretzels and rodent excreta pellets were everywhere.

When the investigator talked to the owner, Shosho Brothers Inc., company officials refused to permit the inspection to continue. The investigator left to make two phone calls and returned about an hour later, accompanied by another FDA investigator and an inspector from the **New York State Department of Agriculture and Markets.** When the officials were advised again of FDA's authority to conduct the inspection and the possible consequences of a refusal, they allowed the inspection to continue. In the meantime, the lot of contaminated pretzels had been removed.

But investigators found more defiled products, this time candy. Rodent pellets were discovered in all four rooms of the warehouse. Structural defects allowed rodents easy access to each storage area.

The U.S. District Court ordered a mass seizure of all food items at the warehouse, and four U.S. marshals served papers on the owners and inventoried all food products on hand.

The firm began repairing the building; rodent entryways were sealed. Food product containers were examined and then moved so storage areas could be thoroughly cleaned. All contaminated products were destroyed at the city dump.

A Rotten Story

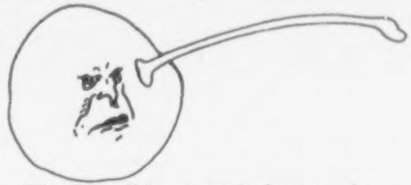
It had been a bad year for the cherry crop in New York and the temptation to use whatever cherries were available, regardless of condition, proved too much for one firm. But FDA was on the spot, and the processed Montmorency cherries ended up in a dump, not in someone's pie.

FDA had been checking processors to be sure that the cherry shortages didn't result in the marketing of unacceptable fruit. Clermont Fruit Packers Inc. of Clermont, N.Y., was busy producing frozen, concentrated cherry pulp when two investigators from the **Albany (N.Y.) resident post** showed up. The plant had only one day of production, and this was the day.

During their inspection, the investigators made nine collections of 100 to 200 cherries each from different parts of the plant and examined them for rot. The samples came from four 55-gallon drums of frozen cherries and from the feeder into which the cherries were being dumped for processing. The plant was making no effort to cull rotten cherries.

FDA allows a small amount of rot in processed cherries because it is considered unavoidable. However, if an average of several samples shows that 7 percent or more of the cherries are rejects (cherries that contain substantial rot), FDA will act to prevent the fruit from being marketed. Of the nine samples, visual examination on the premises revealed that one contained over 23 percent rejects and seven others failed to meet FDA's guidelines. The average rate of rejects was 10.7 percent.

The Buffalo district laboratory examined the samples and confirmed the investigators' findings. On the district's recommendations, the U.S. District Court for the Southern District of New York ordered a U.S. marshal to seize the entire lot of frozen concentrated cherry pulp, consisting of 303 cans weighing 33.5 pounds each.



The firm did not apply for permission to recondition (salvage) the product and the court ordered the lot's destruction. The canned cherries were taken to a landfill dump in Albany by the marshal and buried.

Sad Task

Day after day, workers at Cerveceria India, a brewery in Mayaguez, Puerto Rico, opened can after can of the firm's India brand beer and, mixing it with water, poured it down the drain. This sad task went on for over a year, beginning late in 1980, until 9,124 cases of the brew had been dumped into the Mayaguez sewer system.

The year before, FDA had tested 30 brands of beer and found high levels of nitrosamines, substances that cause cancer in laboratory animals, in Cerveceria India and Tadcaster of England products. The Tadcaster products were refused entry into the United States; the India beer, distributed only in Puerto Rico, was recalled by the firm and destined for destruction.

Nitrosamines can be formed during the drying of green barley to make malt, a basic ingredient of beer. The contamination of the India beer was traced to malt supplied by a mainland U.S. firm.

One reason the dumping took so long was that the brewery was having labor problems during the destruction period. Another was that the Environmental Protection Agency did not want the beer going into the sewer system undiluted, where it could provide a fine yeasty culture for growing molds and other undesirables. EPA required that 105 gallons of water be used to dilute each gallon of beer.

When the last batch went down the drain, Cerveceria India chalked up a $91,000 loss on the value of the beer, plus the costs of the recall and labor required for destruction.

At the time of the FDA tests on the various brands of beer, the average level of nitrosamines for imported beers was 1.9 parts per billion and 3.4 parts per billion for domestic (U.S.) beers. Manufacturers quickly changed their production methods, and within months the nitrosamine content for all beers was averaging an acceptable 1 part per billion.

Juice With a Bang

Unloading bags of groceries in the kitchen is an uneventful chore, but wasn't for a Birmingham, Ala., housewife in December 1981.

While on the counter top waiting to be shelved, a 6-ounce can in a six-pack of Staff brand unsweetened grapefruit juice exploded, spraying a black liquid over the cabinets, the woman's clothing and a kitchen mat.

The consumer called FDA's **Birmingham resident post.** An investigation found that the cause was defective peel-tab seals. Air entering the can around the tab formed a ring of rust about a quarter of an inch below the top rim at the liquid level. The rust caused the juice to turn black. The air pressure inside caused the top to blow off.

Adams Packing Co. of Auburndale, Fla., said there had been problems before with the seals and held that the fault was with the canner, Continental Can Co. of Wintergarden, Fla. Continental also puts the peel tabs on the lids at its Weslaco, Texas, plant. Both components are shipped to Adams for filling and sealing. The packed cans are distributed by the Bruno Grocery Warehouse, Birmingham, to retailers in the area.

FDA visited Bruno's warehouse, checking various product codes of cans to be shipped in interstate commerce. Several lots were found with defective tab seals. U.S. marshals seized the defective cans involved, and Bruno destroyed 430 cases of grapefruit juice, valued at $3,000, on Feb. 17, 1982. Another lot of 416 cases, valued at $2,500, was shipped in error while the investigation was in progress. This, too, was destroyed at Bruno's request.

Digging Up Evidence

In May 1981 FDA recalled about 5 million 4-ounce cans of mushrooms of several code production lots because of botulinum toxin that had been found in several of the cans. Consumers were advised to return any cans of these coded lots to the place of purchase, but one resident of Lawson, Mo., apparently decided to handle it another way. He or she wrapped the cans in a plastic bag and buried them in the back yard.

In March 1982 the new owner of the house unearthed the cache of mushrooms while digging a hole in the yard. An FDA investigator from the **Kansas City district** office matched the codes on the cans with those recalled but was unable to determine why the cans, neatly wrapped in plastic, were interred in the yard. The resurrected cans were reburied in a city landfill, witnessed by FDA.

RIP
1981-1981

Back to Sea for Popeye

An FDA inspector in the **New York district** office was puzzled at the "yellow dye no. 5" ingredient listed on the label of some candy being offered for import from Hong Kong. There is no such color among the additives approved as safe by the agency. The nearest is FD&C Yellow No. 5, but FDA regulations require that manufacturers use that designation in ingredient listings, not something that comes close to it.

The reason FD&C Yellow No. 5 must be identified is that some persons are allergic to it and are entitled to know that color is in a particular food. It is the only food color additive that must be identified so precisely. Other permitted color additives may appear on the label as "artificial color."

The inspector asked the **New York Regional Laboratory** to analyze the candy—lollipops that fitted into plastic handles shaped like Popeye the Sailor and his cartoon character friends. The regional laboratory verified that the candy did contain FD&C Yellow No. 5, a safe and permitted color additive.

But both the laboratory and the inspector noticed another problem. The candy portion of the lollipop could easily break off or slip out of the handle while in a child's mouth. If the candy then lodged in the child's throat, the child might choke.

It resembled an imported candy pacifier that FDA had encountered in 1975 which posed the same kind of hazard for children. The pacifiers had been recalled by the importers, and that is what happened this time. The 5,400 pounds of Popeye Pops, valued at almost $19,000, were sent back to sea.

—This small sample of reports from the field was compiled and written by Marti Asner, Louise Fenner and Richard Thompson.

Seizures and Postal Service Cases

U.S.MAIL

FILED SEIZURE ACTIONS charge violations of the Federal Food, Drug, and Cosmetic Act and are initiated based upon FDA recommendations. A seizure action is commenced by the filing in the U.S. district court where the goods are located. A U.S. marshal is then directed by the court to take possession of the goods, removing the product from commerce, until the matter is resolved.

A total of 8 actions to remove from the consumer market products charged to be violative was reported in July. These actions included 5 of foods: 4 involved charges concerning contamination, spoilage or insanitary handling, and 1 involved economic and labeling violations. Others included 3 of drugs (one of which was a veterinary drug).

PRODUCT, DISTRICT & DATE FILED	FIRM & PLACE OF BUSINESS	CHARGES
	FOOD/Contamination, Spoilage, Insanitary Handling	
Flour and other foodstocks/U.S. District Court for the Southern District of West Virginia 7/14/82	Crook Produce Co./Beckley, W.Va.	Some of the articles contain rodent or bird filth, and all of the articles have been held under insanitary conditions.
Fruit cocktail, canned/U.S. District Court for the Eastern District of Arkansas 6/29/82	Shipped from Tipton, Ind.	Product was held in swollen cans.
Rice, Indian spices, and other Indian foodstocks/U.S. District Court for the Northern District of California 5/28/82	Bombay Bazar Wholesale Distributors/Berkeley, Calif.	Products have been held under insanitary conditions, and some of the products contain rodent and insect filth.
Rice and other foodstocks/U.S. District Court for the Western District of Washington 5/11/82	Mekong Market/Seattle, Wash.	Some of the products contain rodent and/or insect filth, and all of the products were held under insanitary conditions.
	FOOD/Economic & Labeling Violations	
Cranberry-apple drink, "vitamin C enriched"/U.S. District Court for the Eastern District of Louisiana 6/4/82	Derry Products Co./Middletown, N.Y.	A valuable constituent, vitamin C, has been omitted in part, and label is false and misleading in representing that the article contains 45 percent of the U.S. RDA of vitamin C when article contains less.
	DRUGS/Human Use	
Cough syrup/U.S. District Court for the District of New Jersey 7/13/82	Around the World Merchandisers Inc./Linden, N.J.	Product is a new drug without an effective approved New Drug Application; and the labeling falsely represents and suggests the drug contains specific amounts of chloroform, which representation and suggestion are contrary to fact because chloroform is not present in the labeled amounts.
Myco Triacet cream in jars/U.S. District Court for the Western District of New York 6/17/82	Lemmon Co./South Hackensack, N.J.	Circumstances of product's manufacture, processing, packaging and holding were not in conformance with current good manufacturing practice.
	DRUG/Veterinary	
Methenamine tablets/U.S. District Court for the District of Nebraska 6/25/82	Tendene Division, Lee Drug Co./Omaha, Neb.	Product is a new animal drug and no approval of a New Animal Drug Application is in effect with respect to its use or intended use; and the labeling fails to bear adequate directions for use, and the article is not exempted since it is a veterinary prescription drug and it is held to be sold only by prescription.

U.S. POSTAL SERVICE

actions taken in medical cases as authorized in the Mail Fraud Statute (18 U.S.C. 1341) and/or the False Representation Statute (39 U.S.C. 3005) as reported by the Chief Postal Inspector.

Complaints Filed by Law Department Under 39 U.S.C. 3005 (False Representation)

February 23, 1982: **Vita-Health Research,** 1685 Tustin Ave., Costa Mesa, Calif. Advertising and sale through the mail of the product "Thritix." The ad states, in part, "safer than aspirin! New supplement can ease arthritis pain in 10 days . . . in most cases. You don't need stimulants or exotic drugs to find relief."

March 8, 1982: **SPR-1000,** 535 Fifth Ave., New York, N.Y. Advertising and sale through the mail of the product "SPR-1000." The ad states, in part, "once inside your body SPR-1000 is absorbed at once. Their super energized and concentrated protein releases amino acids throughout your body. Once there these amino acids act as a signal that tells your brain's appetite control center that you've absorbed enough nutrition . . . and your body will begin immediately to burn off those unseemly pounds of fat."

March 24, 1982: **Khalid Enterprises,** 9419 Gothic Ave., Sepulveda, Calif. Advertising and sale through the mail of the product "Eyeweights." The ad states, in part, "throw your glasses away. For the first time in history—improve vision without glasses or contact lenses."

March 24, 1982: **Pacific Bio-Khem Ltd.,** P.O. Box 188, Janesville, Wis. Advertising and sale through the mail of the product "Tri-Lemine Diet Tablets," representing the ability to cause weight loss. The ad states, in part, "burns fat faster than exercise . . . your waistline will shrink 3-4 sizes in just two weeks."

March 25, 1982: **Genie Products,** 411 South Sangamon St., Chicago, Ill. Advertising and sale through the mail of the product "Genie Weight Away," representing the ability to cause weight loss. The ad states, in part, "Just wrap it around your waist and your 'spare tire' vanishes. Most important of all, weight away is hard at work (without any effort on your part) making sure that unsightly bulge disappears for good."

April 8, 1982: **Ultra-Slim Inc.,** P.O. Box 281, Roselle, N.J. Advertising and sale through the mail of the product "Frefries," representing the ability to cause weight loss. The ad states, in part, "guaranteed loss of up to 64 pounds of ugly fat in only 8 weeks. No drugs . . . no starvation diets . . . no hunger pains . . . no strenuous exercise . . . and above all, no self control needed."

False Representation Orders Issued by Judicial Officer Under 39 U.S.C. 3005

January 6, 1982: Against **Bradford Warner,** 521 Fifth Ave., New York, N.Y. Satisfactory evidence was presented to the Postal Service that Bradford Warner and its representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Living Fluids and Living Creme," representing the ability to "enlarge your bosom . . . be big busted beautiful in an era of small bosomed women . . . gain up to 6 inches and 3 cup sizes now!"

January 6, 1982: Against **Natures Harvest Inc.,** 95 M South Hoffman Lane, Central Islip, N.Y. Satisfactory evidence was presented to the Postal Service that Natures Harvest Inc. and its agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Super Oxide Dismutase." The ad states, in part, "Anti-aging basics in a bottle . . . taking SOD tablets just might be the easiest way available to fight back at the debilitating effects of free radicals."

January 8, 1982: Against **R. Scott Fitzgerald,** P.O. Box 2700, New York, N.Y. Satisfactory evidence was presented to the Postal Service that R. Scott Fitzgerald and its representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Le Grand Big Bosom Creme and Big Bosom Le Grand Pills," representing the ability to "enlarge your bosom . . . increase your bustline up to 6 inches and 3 cup sizes!"

January 11, 1982: Against **Swedish Extract,** 175 Fifth Ave., New York, N.Y. Satisfactory evidence was presented to the Postal Service that Swedish Extract and its agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Big Bosom Creme." The ad states, in part, "increase your bosom . . . new Swedish discovery . . . adds inches while you sleep. Be the new sexy big size you want to be! Yes, help is finally here for small breasted women."

February 11, 1982: Against **Magnolia Labs,** Box 1306 Pascagoula, Mich. Satisfactory evidence was presented to the Postal Service that Magnolia Labs and its representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Stale Food vs Fresh Food." The ad states, in part, "arteries can cleanse themselves without surgery, by diet alone. A startling new discovery shows how arteries can cleanse themselves without surgery. Just as your skin can cast out thorns your arteries can cast out lumps when you stop forming them with the wrong foods."

February 16, 1982: Against **Charles C. Cunard,** 210 Fifth Ave., New York, N.Y. Satisfactory evidence was presented to the Postal Service that Charles C. Cunard and its agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Placenta Big Bosom Creme and Magnum Cup Expander," representing the ability to "produce gains of six inches and three cup sizes in the female users breast in only ten days . . . will cause the female users breast to gain up to six inches."

February 16, 1982: Against **Lawrence Larrabee,** 663 Fifth Ave., New York, N.Y. Satisfactory evidence was presented to the Postal Service that Lawrence Larrabee and its representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Aero-Plus 3." The ad states, in part, "enlarge your bosom 3 full cup sizes in only 7 days!"

February 17, 1982: Against **Clifton Pharmacal Wholesale Inc.,** Box 43, Milroy, Pa. Satisfactory evidence was presented to the Postal Service that Clifton Pharmacal Wholesale Inc. and its agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising "Stimulants." These stimulants are being sold as look-alike narcotics.

February 25, 1982: Against **Brant Pharmacal,** P.O. Box 922, Toledo, Ohio. Satisfactory evidence was presented to the Postal Service that Brant Pharmacal and its representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising "Stimulants." These stimulants are being sold as look-alike narcotics.

March 2, 1982: Against **Standard Research Labs,** P.O. Box 9547, Fort Lauderdale, Fla. Satisfactory evidence was presented to the Postal Service that Standard Research Labs and its representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Bio-Prima II," representing the ability to "yield a cure for baldness. 80% of those treated regrew hair from using Bio-Prima II."

March 2, 1982: Against **Cosvetics,** P.O. Box 11627, Atlanta, Ga. Satisfactory evidence was presented to the Postal Service that Cosvetics and its representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Bio-Genesis." The ad states, in part, "the most amazing anti-baldness product ever developed. No matter what you've heard about baldness before, that it's hereditary, permanent, etc., can be thrown out the window. With this brochure, you will find the ability to stop excessive hair fall out and generate new hair growth, even in individuals who have been bald for over 20 years."

March 15, 1982: Against **Phun Pharmaceuticals,** P.O. Box 2118, Gaithersburg, Md. Satisfactory evidence was presented to the Postal Service that Phun Pharmaceuticals and its agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising "Stimulants." These stimulants are being sold as look-alike narcotics.

Notices of Judgment

NOTICES OF JUDGMENT on Seizure Actions

FOOD/Contamination, Spoilage, Insanitary Handling

Mole en pasta, at Chicago, N. Dist. Ill.

Charged 3-30-82: when shipped by Alejandro Herrera, Chicago, Ill., from Los Angeles, Calif., the article, labeled in part "Mole en pasta—Dona Maria . . . Hecho En Mexico Por: Productos Dona Maria, S.A., " contained insect and rodent filth—402(a)(3); and required label information was not in such terms likely to be read and understood under customary conditions since such information was in Spanish rather than English—403(f). Default decree ordered destruction. (F.D.C. No. 63680; S. No. 82-314-730; N. J. No. 1)

Mole en pasta, at Chicago, N. Dist. Ill.

Charged 4-16-82: when shipped from outside Illinois, the article, labeled in part "Mole en pasta—Dona Maria . . . Hecho En Mexico Por: Productos Dona Maria, S.A.," contained insect, rodent, bird and animal filth—402(a)(3); and required label information was not in such terms likely to be read and understood under customary conditions since such information was in Spanish rather than English—403(f). Default decree ordered destruction. (F.D.C. No. 63699; S. No. 82-314-683; N.J. No. 2)

Rice, at Guaynabo, Dist. Puerto Rico.

Charged 4-8-82: while held by Rice Growers Association of California (Puerto Rico) Inc., Guaynabo, Puerto Rico, the article contained insect filth and had been held under insanitary conditions; 402(a)(3), 402(a)(4). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63701; S. No. 82-274-792; N.J. No. 3)

Rice powder, dried fish, chrysanthemum tea, and **other stocks of Oriental foods,** at Seattle, W. Dist. Wash.

Charged 1-29-82: while held by Yick Fung, Seattle, Wash., several lots of food (soup base, cane & arrowroot stock, rice powder, chrysanthemum tea and dried fish) contained insect filth, and all of the articles had been held under insanitary conditions; 402(a)(3), 402(a)(4). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63637; S. No. 82-279-112; N.J. No. 4)

Salt, and **rice,** at Miami, S. Dist. Fla.

Charged 6-23-82: while held by West Indies Food and Packing Inc., Miami, Fla., the salt contained rodent filth, the rice contained insects, and the articles had been held under insanitary conditions; 402(a)(3), 402(a)(4). Default decree ordered destruction. (F.D.C. No. 63261; S. No. 81-166-313; N.J. No. 5)

Sauce, mexican hot, at El Paso, W. Dist. Texas.

Charged 3-30-82: when shipped from Mexico, the article contained insect and rodent filth; 402(a)(3). Default decree ordered destruction. (F.D.C. No. 63683; S. No. 82-266-691; N.J. No. 6)

Spaghetti, and **macaroni product,** at Rochester, W. Dist. N.Y.

Charged 1-18-82: while held by Olindo Imported Foods Inc., Rochester, N.Y., the articles had been held under insanitary conditions; 402(a)(4). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63617; S. No. 82-284-922; N.J. No. 7)

FOOD/Economic and Labeling Violations

"Maple" syrup, Pure Pioneer, at Phoenix, Dist. Ariz.

Charged 4-8-82: when shipped by Dewey Clark, Philadelphia, Miss., corn syrup had been substituted for maple syrup—402(b)(2); the article's labeling was false and misleading because of representations that the food consisted wholly of maple syrup—403(a)(1); the article failed to conform to the definition and standard of identity for maple syrup because the article was made with syrup derived from a source other than the maple tree—403(g)(1). Default decree authorized release to a charitable institution. (F.D.C. No. 63698; S. No. 82-306-223; N.J. No. 8)

"Orange juice" for manufacturing, concentrated (COJM), at Chicago, N. Dist. Ill.

Charged 7-18-81 and amended 11-19-81: when shipped by Citro-Florida Inc., San Antonio, Texas, the article's valuable constituent, orange juice, had been omitted or abstracted and other substances had been substituted (e.g., turmeric, liquid sugar, ammonium citrate, potassium citrate, ascorbic acid, and citric acid)—402(b)(1); the color additive turmeric had been added to make the article appear better or of greater value than the article was—402(b)(4); and the article contained the non-conforming color additive turmeric, since no regulation permitted its addition to concentrated orange juice for manufacturing—402(c); the article's labeled name "COJM" falsely and misleadingly represented the article as concentrated orange juice for manufacturing when the article was not because it contained artificial color (i.e., turmeric, annatto and other specified substances)—403(g)(1); and the article contained the artificial coloring turmeric and annatto and its label failed to state that fact—403(k).

The article was claimed by the shipper. By its first supplemental answer and claim, the claimant admitted that FDA found turmeric in the tested drums, made no claim of ownership to those drums of "COJM" but claimed ownership of the other drums. The government moved to take the claimant's deposition. The claimant opposed such motions by moving to quash. The government moved to compel the claimant's testimony. The claimant stated that it no longer desired to claim the article and had no objection to dismissing the claimant from the action. The claimant then moved to quash the notice of depositions and motions to compel testimony based on its withdrawal of its claim. The court adjudged the default of all persons having an interest in the article, adjudicated the charges in favor of the government, ordered the article destroyed or donated to a charitable institution, and decreed that the claimant pay storage costs. Citro-Florida Inc. moved to amend the decree, claiming that the decree erroneously referred to Citro-Florida Inc. as "claimant" in the present tense, and objecting to the payment of costs.

The court denied the motion of Citro-Florida Inc., saying:

"Citro-Florida, Inc.'s Motion to Amend the portion of this court's judgment which required movant to pay the costs of storage of certain seized articles incurred between Sept. 2, 1981, and Feb. 12, 1982, is denied.

"The court's decision is mandated by 21 U.S.C. §344 (e) which

provides as follows: '(e) When a decree of condemnation is entered against the article, court costs and fees, and storage and other proper expenses, shall be awarded against the person, if any, intervening as claimant of the article.'

"Citro-Florida, Inc. was a claimant in this action until Jan. 21, 1982, on which date its motion to withdraw its claim to the seized goods was granted. On Feb. 12, 1982, this court entered a Default Decree of Condemnation which required, in part, that Citro-Florida, Inc. 'pay the costs of storage of the seized articles between Sept. 2, 1981, and this date.'

"Citro-Florida, Inc. now argues that because its claim to the seized goods was withdrawn on Jan. 22, storage costs could not be assessed against it on Feb. 12. Its reasoning is that §334(e) only applies to a party who is still in the case as a claimant at the time the decree of condemnation is entered. This court disagrees.

"It is the court's conclusion that Citro-Florida, Inc.'s reading of §334(e) is erroneous. A proper interpretation of the statute has been provided by Judge Blair of the U. S. District Court for the District of Maryland. In *United States* v. *Articles of Drug . . . Penapar VK*, 458 F. Supp. 687 (D.Md. 1978), Judge Blair stated, 'The statute does not provide for the payment of costs only after the decree of condemnation and only by the party *then* intervening as claimant. It is true that the award of costs is to be made at the time the decree of condemnation is entered. However, the statute mandates an award of costs against any person intervening as claimant in the proceeding; there is no requirement expressed in §334(e) that the person against whom costs are awarded still be a party to the proceeding at the time the decree is entered.' 458 F. Supp. at 688. The court continued by stating that an interpretation like that offered by Citro-Florida, Inc. 'would allow an unsuccessful claimant to avoid the award of costs under §334(c) by merely withdrawing its claim prior to the entry of the condemnation decree.' *Id.* at 689. That, this court believes, should not be allowed.

"Citro-Florida, Inc. also argues that once its claim was withdrawn, this court no longer had jurisdiction over the company so as to permit the court to assess storage costs against it. This assertion cannot be accepted. Withdrawal of plaintiff's claim ended any dispute regarding the condemnation and destruction. The entry of the decree of condemnation and the court's order requiring Citro-Florida, Inc. to pay costs were merely procedural formalities implementing the court's order of Jan. 21, 1982. The procedure followed is clearly contemplated by the statute, *see, United States* v. *Articles of Drug . . . Penapar VK, supra.*, and is fully appropriate. *Cf.* Rule 58. (' . . . Entry of the judgment shall not be delayed for the taxing of costs . . . '). Furthermore, this court believes that the cases cited by plaintiff are inapposite. Citro cites *Consumers Union of U.S., Inc.* v. *Consumer Product Safety Commission*, 590 F.2d 1209 (D.C. Cir. 1978), *rev'd on other grounds*, 445 U.S. 375 (1980) and *Zenith Radio Corp.* v. *Hazeltine Research, Inc.*, 395 U.S. 100 (1969). These cases hold no more than that a court's judgment does not affect a person who was never served and had never appeared in the action in any manner. That is a far different case from the instant one where it is undisputed that Citro was a claimant and had appeared in the action. In such a situation, this court believes that the court's order that Citro-Florida, Inc. pay storage costs was proper and should not be amended.

"For the foregoing reasons, Citro-Florida, Inc.'s Motion to Amend the Judgment is denied." (F.D.C. No. 63511; S. No. 81-291-205; N.J. No. 9)

DRUGS/Human Use

Butabarbital, acetaminophen & aspirin combination elixir, at Greensboro, M. Dist. N.C.

Charged 4-22-81: when shipped by Huen/Norwood Div., The Mogul Corp., St. Louis, Mo., the article, labeled in part "Sedapap Elixir . . . Analgesic—Antitensive Antipyretic . . . Mfg. for Mayrand Incorporated Pharmaceuticals Greensboro, N.C.," was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (F.D.C. No. 63421; S. No. 81-190-585; N.J. No. 10)

Butalbital, phenacetin & aspirin (combination) capsules, at Greensboro, M. Dist. N.C.

Charged 4-22-81: when shipped in bulk by D. M. Graham Laboratories Inc., Hobart, N.Y., and thereafter repacked into 100-capsule bottles labeled in part "Buff-A-Comp Caps . . . Graham Labs, Hobart, N.Y. . . . Mfg. for Mayrand Incorporated Pharmaceuticals Greensboro, N.C.," the article was a new drug without an effective approved New Drug Application; 505(a). Default decree ordered destruction. (F.D.C. No. 63440; S. No. 81-251-634; N.J. No. 11)

Dexamethasone acetate & dexamethasone sodium phosphate combination injectable, at Maryland Heights, E. Dist. Mo.

Charged 6-9-81: when shipped by Carter-Glogau Laboratories Inc., Glendale, Ariz., the article, labeled in part "Dalalone R.P. . . . O'Neal Jones & Feldman, St. Louis, Mo.," was a new drug without an effective approved New Drug Application; 505(a). Consent decree ordered destruction. (F.D.C. No. 63479; S. No. 81-123-574; N.J. No. 12)

Hydroxyzine HCl tablets, and **prochlorperazine capsules,** at Newington, Dist. Conn.

Charged 10-22-79: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). Pursuant to stipulation, the action was transferred to the Eastern District of New York for trial with a similar action. Subsequently, a consent decree ordered destruction. (F.D.C. No. 62447; S. No. 79-133-260; N.J. No. 13)

Sodium salicylate tablets, at Camden, Dist. N.J.

Charged 1-28-81: when shipped by Richlyn Laboratories Inc., Philadelphia, Pa., the circumstances used for the article's manufacture, processing, packing and holding failed to conform with current good manufacturing practice; 501(a)(2)(B). Default decree ordered destruction. (F.D.C. No. 63580; S. No. 81-274-129; N.J. No. 14)

MEDICAL DEVICE

Scalp stimulators, electrical, at Buffalo, W. Dist. N.Y.

Charged 11-21-80: the labeling lacked adequate directions for use, and adequate directions could not be written for the devices' labeled purposes (i.e., for hair regrowth in male pattern baldness), the labeling lacked adequate warnings against unsafe use, and the devices had been manufactured in an unregistered establishment; 502(f)(1), 502(f)(2), 502(o).

The article was claimed by Beach Holding Corp., Buffalo, N.Y. The government served written interrogatories on the claimant, and a request for the production of documents. Subsequently, the government moved to compel answers to the discovery requests. The claimant failed to appear and the court ordered that the claimant's answer be stricken. The court rendered a default decree in favor of the government, ordering that FDA might utilize the article as it deemed necessary for demonstration purposes. (F.D.C. No. 62865; S. No. 80-174-923; N.J. No. 15)

NOTICES OF JUDGMENT on Criminal Actions

Fred C. Dalton, M.D., clinical investigator, Mineola, E. Dist. N.Y.

Charged 5-6-82: that the defendant knowingly and willfully failed to establish and maintain adequate and accurate records for a Dothiepin HCl clinical investigation study, in that false ophthalmological examination results were placed in patient case histories when in fact such ophthalmological examinations were not performed or, if performed, were not performed as part of the Dothiepin HCl study—505(i); and that defendant knowingly and willfully failed to establish and maintain adequate and accurate records for a Dothiepin HCl clinical investigation study, in that false laboratory test results were placed in patient case histories when such laboratory tests had not been performed or, if performed, had not been performed as part of the Dothiepin HCl study—505(i). Guilty plea; $1,000 fine. (F.D.C. No. 62430; S. No. 79-185-125; N.J. No. 16)

Emil Lerch, cannery operator, Hatfield, E. Dist. Pa.

Charged 4-20-80 by grand jury: that the defendant caused cannery employees to place stamped notations on No. 10 cans of recalled canned mushrooms so as to represent that such cans had been reprocessed, although the defendant knew such cans had not been heat-processed as required by the cannery-proposed and FDA-approved reprocessing plan; that the defendant caused the cannery employees to generate fictitious charts and logs which purported to document the heat-processing of certain cans, although the defendant knew that the cans had not been heat-processed; that, in a matter within FDA jurisdiction, the defendant knowingly and willfully made false representations to FDA by furnishing fictitious charts which purported to document the heat-processing on Dec. 16, 1980, and on Dec. 24, 1980, of certain cans of mushrooms which had not been heat-processed—18 U.S.C. 1001; that, when shipped to Springfield, Mass., cans of mushrooms had been stamped "1216 RPG," knowingly and willfully representing, with intent to mislead, that they had been reprocessed when in fact they had not been reprocessed—403(a)(1); and that, when shipped to Atlantic City, N.J., cans of mushrooms had been stamped "1217 RPA," knowingly and willfully representing, with intent to mislead, that they had been reprocessed when in fact they had not been reprocessed—403(a)(1). Guilty plea; $28,000 fine and probation for three years. (Misc. No. 652; S. No. 81-228-540 et al.; N.J. No. 17)

NOTICES OF JUDGMENT on Injunction Actions

Dan H. Miller, t/a Dan's Dairy, Burlington, W. Dist. Wash.

Charged 1-29-80 in a complaint for injunction: that the defendant had been, at his dairy, procuring, holding, treating as necessary with veterinary drugs, and offering for slaughter cows whose meat and edible organs contained non-conforming drugs; that such meat and edible organs had been held under insanitary conditions whereby their meat and/or edible organs might be rendered injurious to health since the animals had been treated with new animal drugs contrary to the directions in the labeling and had not been properly withheld from slaughter for the prescribed length of time to permit depletion of drug residues; that the U.S. Department of Agriculture reported its examination of tissue samples of the flesh and/or organs of cattle offered for slaughter by the defendant revealed the presence of new animal drug residues in excess of allowable tolerances; that FDA analyses qualitatively confirmed violative drug residues in each tissue sample except one; that the defendant's cows were offered for slaughter to meatpacking firms selling meat to a variety of retail and wholesale food stores and to other manufacturers of meat products, including firms selling meat and meat products in interstate commerce; that FDA inspections disclosed the defendant failed to maintain adequate records of his use of drugs in cattle subsequently offered for slaughter; and that the defendant was well aware his activities were in violation of the law; 402(a)(2)(D), 402(a)(4).

A consent decree of permanent injunction enjoined the complained of violations and enjoined offering for sale, whether or not directly for slaughter, any cattle whose meat might subsequently be shipped in interstate commerce unless and until a number of specified methods, facilities and controls had been established, operated and administered at the defendant's dairy to assure no new animal drug residue or (if a tolerance has been established) no residue in excess of the tolerance, and unless and until appropriate records of any cattle on hand had been prepared, FDA had been notified, and FDA notified the defendant in writing that he appeared to be in compliance. (Inj. No. 921; U.S.D.A. No. 484415 et al.; N.J. No. 18)

Oriental Foods Inc., and **Tony Kajiwana,** president, **Yosh Nakayama,** vice president, and **Roy T. Nagai,** secretary-treasurer, Denver, Dist. Colo.

Charged 11-23-76 in a complaint for injunction: that the defendants prepared, packed, held for sale (after interstate shipment of the raw ingredient beans) and distributed in interstate commerce mung bean sprouts which contained *E. coli* and excessive total bacteria and which had been prepared, packed and held under insanitary conditions; that FDA inspections revealed a number of specified insanitary conditions and practices; and that the defendants had been repeatedly warned by FDA of insanitary conditions and practices at their plant; 402(a)(3), 402(a)(4).

A consent decree of permanent injunction enjoined continued plant operation involving interstate food unless and until a number of specified methods, facilities and controls were established, operated and administered in conformity with practices which would assure that no food was contaminated with bacterial filth; and unless and until all food on hand at the plant was examined and all contaminated food was destroyed or otherwise brought into compliance. (Inj. No. 746; S. No. 77-72-969 et al.; N.J. No 19)

Tar Heel Veterinarian Supply Inc., and **Rufus Nelson Leonard**, president, and **Barbara Newton Leonard**, secretary-treasurer, Wake Forest, E. Dist. N.C.

Charged 1-3-79 in a complaint for injunction: that the defendants had held for sale after interstate shipment and had been shipping in interstate commerce various drugs, including the prescription veterinary drugs phenylbutazone injection, promazine granules, and procaine penicillin injection; that the defendants were not lawfully engaged in the storage and wholesale and retail distribution of prescription veterinary drugs since they were neither licensed as pharmacists or assistant pharmacists nor registered to dispense prescription veterinary drugs, as required by state authority; that the labeling of the defendants' drugs lacked adequate directions for use as defined by regulations since the drugs were prescription veterinary drugs and were not exempted because they were not sold properly; that FDA investigators, posing as individual customers, had made a number of purchases of such drugs without a veterinarian's prescription; that FDA inspections and reviews of invoices indicated that the defendant firm routinely made shipments of prescription veterinary drugs without a veterinarian's prescription; and that the defendants had been warned against, and were aware of, the illegality of the sale of prescription veterinary drugs without a prescription; 502(f)(1).

A consent decree enjoined the complained of violation and enjoined any interstate business in prescription veterinary drugs unless and until procedures and files were established which would relate every such sale of a prescription veterinary drug to a veterinary prescription, unless and until the defendants demonstrated that they were properly registered or licensed under state law, and unless and until the defendants established and maintained prescription veterinary drug records and files in such a manner that the firm's inventory and the quantity of prescription veterinary drugs received could be reconciled with the quantity of dispensed drugs. (Inj. No. 880; S. No. 78-100-159; N.J. No. 20)

NOTICE OF JUDGMENT on Miscellaneous Action

P. Mastrippolito & Sons Inc., and **Nick Mastrippolito Jr.**, agent of mushroom distributor and sometime cannery, Embreeville, E. Dist. Pa.

Charged 10-12-80 in an order to show cause: that the defendants appear to show cause why they should not be held in contempt of court for failing to permit FDA inspector Larry Fish or any other FDA investigator to enter the defendants' premises in order to inspect the establishment pursuant to court order.

The defendants moved to quash. Subsequently, pursuant to stipulation of the parties, FDA was authorized to inspect the wholly owned subsidiary corporation Kay's Mushrooms Inc., and FDA withdrew its contempt petition, which was dismissed without prejudice. The defendants agreed to notify FDA upon their resumption of the canning or packing of mushrooms or other food products and agreed to permit FDA inspection after such notification. (Misc. No. 632; N.J. No. 21)

Notices of Judgment are given pursuant to section 705 of the Federal Food, Drug, and Cosmetic Act. Notices of Judgment report cases involving seizure proceedings, criminal proceedings, and injunction proceedings. Seizure proceedings are civil actions taken against *goods* alleged to be in violation, and criminal and injunction proceedings are against *firms* or *individuals* charged to be responsible for violations. The cases generally involve foods, drugs, devices, or cosmetics which were alleged to be adulterated or misbranded or otherwise violative of the law when introduced into and while in interstate commerce, or while held for sale after shipment in interstate commerce.

Notices of Judgment are prepared by Food and Drug Division, Office of the General Counsel, HHS.

Published by direction of the Secretary of Health and Human Services.

Arthur Hull Hayes Jr., M.D., *Commissioner of Food and Drugs*
Washington, D.C., Oct. 1, 1982

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Section 705[375] of the Food, Drug, and Cosmetic Act: (a) The Secretary shall cause to be published from time to time reports summarizing all judgments, decrees, and court orders which have been rendered under this Act, including the nature of charge and the disposition thereof.

(b) The Secretary may also cause to be disseminated information regarding food, drugs, devices, or cosmetics in situations involving, in the opinion of the Secretary, imminent danger to health, or gross deception of the consumer. Nothing in this section shall be construed to prohibit the Secretary from collecting, reporting, and illustrating the results of the investigations of the Department.

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Are you reducing your risk of heart attack?

Most coronary risk factors are preventable, curable or treatable. Do you know the most common risk factors?

Test yourself. Find out how much you know about preventing a heart attack.

This is not a pass or fail test. Its purpose is to tell you how much you know about reducing your risk of a heart attack.

1 Which is a major risk factor to heart attack?

a High blood pressure.
b Cigarette smoking.
c High levels of cholesterol and fat in the blood.
d Diabetes.
e All of the above.

2 Which additional factor may contribute to your risk of heart attack?

a Obesity.
b Family history of heart disease.
c Lack of regular exercise.
d All of the above.

3 Which health risks are most controllable by the individual?

a Risks related to your behavior and habits.
b Inherited traits.
c Problems in your environment, such as air pollution, highway conditions.
d Conditions that require care from hospitals, doctors and other health professionals.

4 If you feel uncomfortable pressure, shortness of breath or pain in the center of your chest lasting 2 minutes or more:

a Drive yourself to a hospital immediately.
b Wait an hour, it may be heartburn or indigestion.
c Call an emergency rescue service.
d Leave a message with your doctor's answering service.

5 Which foods *add* to cholesterol in the blood?

a Polyunsaturated vegetable oils and margarine.
b Low-fat milk and yogurt.
c Egg yolks, butter and cheese.
d Fish and poultry.

6 A stroke happens when oxygen-rich blood is cut off on its way to the brain. Warning signals of stroke include:

a Temporary dimness or loss of vision, particularly in one eye.
b Unexplained dizziness, unsteadiness or sudden falls.
c Sudden, temporary weakness or numbness on one side of the body.
d Temporary loss of speech.
e All of the above.

7 Anyone starting a program of regular exercise for cardiovascular fitness should:

a Go "all out" from the start.
b Constantly push to increase the intensity of activity.
c Pick activities which are rhythmic and repetitive. Start slowly.
d Always stand still or lie down immediately after exercising.

8 Hypertension means:

a Being nervous and high-strung.
b Feeling very tense.
c Having blood pressure that stays higher than normal.
d All of the above.

9 Untreated, high blood pressure can cause which problem?

a Stroke.
b Heart attack.
c Kidney failure.
d All of the above.

10 If you have high blood pressure, you will need to:

a Take medications as prescribed.
b Get your blood pressure checked regularly.
c Decrease amount of sodium (salt) you eat.
d Lose weight if overweight.
e All of the above.

ANSWERS:

(1)*e* (2)*d* (3)*a* (4)*c* (5)*c*
(6)*e* (7)*c* (8)*c* (9)*d* (10)*e*

Score 10 points for each correct answer.

100 or 90 — Excellent: Your answers show you're aware of the risk factors for avoiding a heart attack. Just remember, you can call Red Cross anytime anyone in your family needs health instruction.

80 or 70 — Good: But, there's room for improvement. Call Red Cross for a listing of the health and safety courses available at your local chapter.

60 or below — You need help! Learn how to take better care of your heart. Call your nearest Red Cross chapter.

Countless lives have been saved through safety and health skills learned through Red Cross courses. And because of these skills, millions of Americans live safer, happier, healthier lives.

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November 1982

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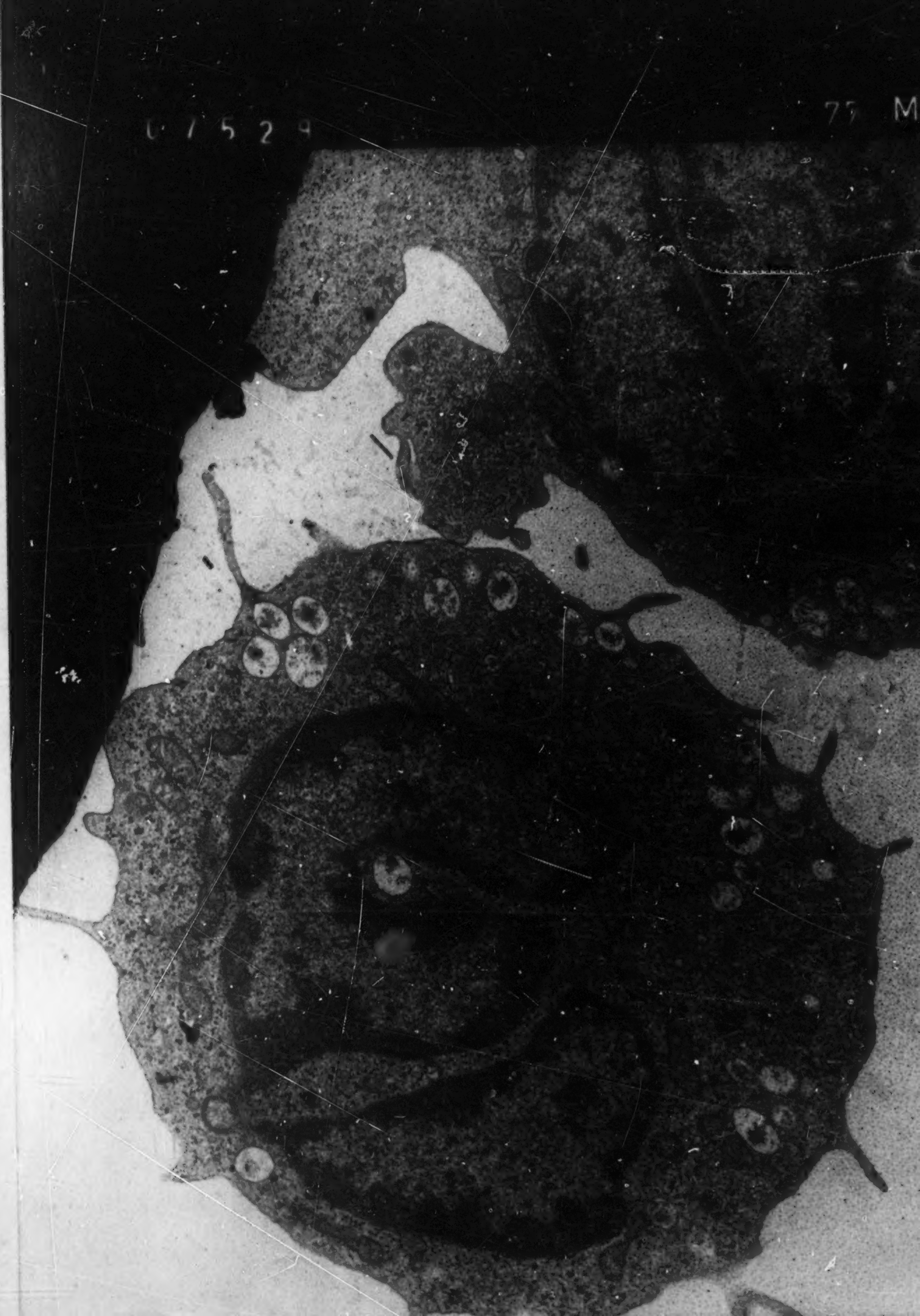
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VOL. 16 NO. 9 NOVEMBER 1982

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Current That Switches Off Pain 5
Through-the-skin electrical stimulation can relieve some types of chronic or acute pain for some people. For these, personal stimulating devices are available only by prescription.

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Mercury lamps provide light cheaper than ordinary tungsten bulbs for gymnasiums and other uses, but breaks and defects can release harmful ultraviolet radiation unknown to the persons exposed. FDA standards contain built-in safety factors for mercury lamps where risk of exposure is greatest.

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Shown here at high magnification is one of the body's guardians against invaders, a white blood cell. Billions of them float in the bloodstream along with red cells—which run in the trillions—and platelets. To learn more about what's in blood and what happens to it inside and out of the body, see Blood: A Fluid You Can Bank On, *on page 10.*

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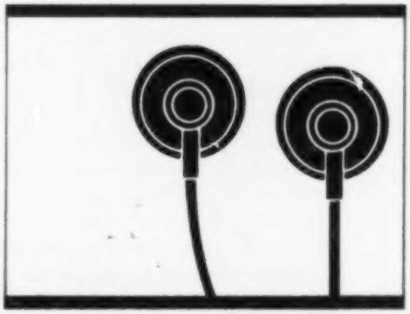

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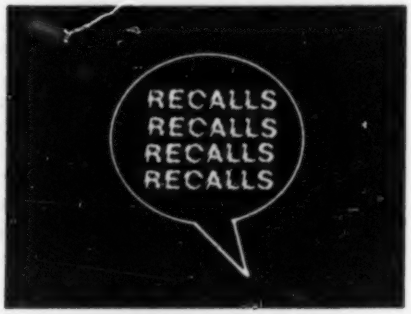

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Updates

Dangerous Drug Masquerade

Look-alike street drugs have a new look. This time they are masquerading as novelty "cocaine." FDA has warned users of these substitutes that they can be as deadly as the high-priced originals.

The agency has received reports of three deaths associated with injecting or sniffing these substitute white powders, many of which contain local anesthetics such as lidocaine, procaine and tetracaine.

The substitutes are sold openly by mail and in "head shops" as novelty "cocaine" or incense under such names as Toot, Florida Snow, Supercaine, Ultracaine, Base-O-Caine and SuperiorCaine.

Last year's look-alikes were bogus stimulants and sedatives ("uppers" and "downers") containing legal drugs such as phenylpropanolamine, caffeine and ephedrine. (See "On the Trail of Counterfeit Drugs," *FDA Consumer*, December 1981-January 1982.)

The main dangers of the cocaine substitutes are that they can cause blood vessels to collapse, depress heart muscle strength and cause low blood pressure.

Because of cocaine's high abuse and dependency potential, it is regulated under the Controlled Substances Act by the Drug Enforcement Administration. Cocaine substitutes are not controlled under that act and are subject to FDA regulation under the Federal Food, Drug, and Cosmetic Act.

FDA has notified manufacturers of the types of anesthetics used in cocaine substitutes about its concern over this public health problem. The manufacturers are being asked to impose stringent controls over the distribution of the bulk anesthetics to assure that they are offered for sale only to legally authorized firms.

Warning for Pregnant Women

Pregnant and nursing women will be warned to seek professional advice before using most non-prescription drugs, under an FDA proposal. The warning would state: "As with any drug, if you are pregnant or nursing a baby, seek professional advice before using this product."

The warning would be required on over-the-counter (OTC) drugs that are absorbed by the body but would not be required on most externally applied products such as salves or liniments.

For certain OTC drugs, FDA had previously established specific warnings for use by pregnant or nursing women. These warnings were based on scientific data that suggested a potential hazard to developing or newborn children. For those drugs, the specific warnings would apply, rather than the standard warning proposed.

But even when there are no data to suggest that particular OTC drugs present a potential hazard, there also may be no data demonstrating that such drugs are safe when used by pregnant or nursing women.

The proposal appeared in the Sept. 7 *Federal Register*. FDA accepted public comments on the proposal for 30 days.

The state of California had previously set a similar warning for non-prescription drugs sold in that state.

'Legal Stimulants' Seized

At the request of the Food and Drug Administration and the Department of Justice, U.S. marshals seized thousands of so-called "legal stimulants" containing non-prescription drug ingredients at three manufacturers during the last two weeks of August.

The seizures followed FDA's notification of 16 manufacturers in August that they must discontinue marketing drugs containing the combination of caffeine (a stimulant), phenylpropanolamine (an appetite suppressant) and ephedrine (a decongestant). FDA advised the manufacturers that the triple combination requires approval by FDA before it can be marketed.

The products, advertised as "100 percent legal" pep pills and speed, have been distributed nationwide and promoted through ads in campus newspapers, the mail and handbills at truckstops, schools and rock concerts.

FDA medical experts determined that the combination of the three ingredients is irrational and not generally recognized as safe and effective for use under the conditions suggested in the labeling. In combination, or when taken in excessive doses, these ingredients may cause illness or death. They may, for example, raise blood pressure to the point of causing cerebral hemorrhage.

The seizures were made after FDA investigators found drugs with these three ingredients at the plants. The three firms were: B. T. Products Inc., Tampa, Fla.; Pharmafair Inc., Hauppauge, N.Y.; and Pharmaceutical Dynamics Inc., Hauppauge, N.Y.

The seizures netted over one million finished capsules and tablets and more than $100,000 worth of machinery used in their manufacture.

Nearly a year earlier, U.S. marshals and FDA agents had seized large quantities of "look-alike" pep pills containing various combinations of these ingredients at nine factories in five states. The seizures were requested by FDA because the drugs were counterfeits of various abused prescription-controlled substances commonly sold on the street. Currently, at least 35 states have passed legislation concerning the distribution of the "look-alike" pills. (See "On the Trail of Counterfeit Drugs" in the December 1981/January 1982 *FDA Consumer.*)

Since then, the non-look-alike drug products containing the same ingredients had become increasingly popular. These products no longer look like amphetamines or other controlled substances but are being sold on an illicit market of their own.

FDA has worked closely with the Drug Enforcement Administration, U.S. Postal Service and other federal agencies, and has encouraged and supported state attempts to deal with this drug abuse problem.

Underarm Safety

Aluminum chlorohydrate in aerosol form is safe as an antiperspirant, FDA has decided. This means that this ingredient won't have to undergo further testing to assure its safety, as an advisory panel of experts recommended back in 1978. Because of concern that continued use of aerosol sprays may present a potential health hazard, the panel had called for long-term inhalation studies with animals. The panel's recommendations were discussed in "Aerosol Antiperspirants: Under a Cloud" in the November 1978 *FDA Consumer.*

FDA's decision regarding aerosol antiperspirants was made public by the Aug. 20 *Federal Register* publication of a proposed monograph, or standard, for this class of over-the-counter (OTC) drugs. The agency's conclusions were based on an evaluation of the recommendations of the Advisory Review Panel on OTC Antiperspirant Drug Products and on public comments on the panel's report. The antiperspirant monograph was one of three proposed during August. Monographs for anthelmintic and cholecystokinetic drug products were published Aug. 24.

FDA agreed with the antiperspirant panel's recommendations that non-aerosol forms of aluminum chlorohydrates, aluminum chloride, aluminum zirconium chlorohydrates and buffered aluminum sulfate also should be considered safe and effective antiperspirant ingredients. However, the agency did not accept a panel recommendation that a minimum effectiveness statement must appear on the label of these products. Such a statement would not serve its intended purpose, said FDA. The agency also expanded the labeling to provide for a wider variety of allowable statements in addition to the panel's lone choice of "reduces underarm perspiration."

The statement "apply to underarms only" replaces the phrase "not to be used generally over the body" in FDA's proposed labeling for antiperspirants. Aerosol products should be labeled with the warning "avoid excessive inhalation," the agency proposed.

In the matter of anthelmintic drug products, FDA disagreed with the view of the Advisory Review Panel on OTC Miscellaneous Internal Drug Products that gentian violet is safe and effective for treating pinworms. This ingredient is a potential carcinogen, the agency said in its monograph. The agency did agree, however, that pyrantel pamoate should be moved from prescription to non-prescription status and that piperazine citrate should not be allowed in pinworm drugs.

Labeling for anthelmintic drugs should clearly state that the product is for the treatment of pinworms and should warn against use by those who have liver disease. Although the directions for use indicate that the entire household should be treated when one person in a family has pinworms, FDA included in its proposed monograph a warning that pregnant women should take the medicine only if they have pinworms themselves or are directed to take it by a doctor.

Cholecystokinetic drugs are used to contract the gallbladder during diagnostic gallbladder studies. FDA and the Miscellaneous Internal Drug Panel agree that the only ingredient for this use is a 50 percent aqueous emulsion of corn oil. The agency also agrees with the panel that this product should be available as a non-prescription drug even though it is to be used under the direction of a doctor.

Publication of a proposed monograph is the next to last stage in FDA's massive review of ingredients in all non-prescription drugs. Final standards will be published after public comments on the proposed monographs have been evaluated. Final standards for antiperspirants and cholecystokinetic drugs will become effective 12 months after publication, while standards for anthelmintics will become effective six months after publication.

Whooping Cough Epidemic

Last September the British health department launched a publicity campaign to persuade parents to have children vaccinated for whooping cough. The move was in response to the worst epidemic of whooping cough to strike Britain in 25 years.

Government figures for the week ending Sept. 4, 1982, showed 2,267 new cases of whooping cough and reported the total for the year at 35,497. Four babies were reported to have died as a result of the highly contagious disease in the first seven months of the year.

In comparison, 58 cases of whooping cough (pertussis) were reported in the United States to the national Centers for Disease Control during the week ending Sept. 4, with 938 cases for the year.

The British health department attributed the epidemic to low vaccination levels that resulted from public fear about the safety of the pertussis vaccine in the mid-1970s. As a result of publicity about brain damage detected in a small number of vaccinated babies, vaccination levels in Britain plummeted from 80 percent of all babies to 31 percent in 1978. Levels gradually climbed to 45 percent in 1981.

In the United States, public concern over the risk of side effects from pertussis vaccine surfaced in April 1982, following a television documentary by the National Broadcasting Co.'s Washington, D.C., outlet and publicity on NBC's "Today Show." FDA Commissioner Arthur Hull Hayes Jr. was interviewed in a follow-up news segment by the NBC Washington station. A transcript of that interview was published in the July-August 1982 *FDA Consumer*.

Arthritis Drug Withdrawn

Lilly Industries Ltd. surrendered its licenses to market the arthritis drug Opren (benoxaprofen) in the United Kingdom early in September. The drug, marketed as Oraflex in the United States, was suspended worldwide by Lilly on Aug. 4 after the United Kingdom halted its sale with a 90-day license suspension as a result of 61 deaths possibly associated with the product there.

Lilly was making arrangements to recall all existing supplies of the product and has advised pharmacists and doctors by letter to halt the drug's use. FDA announced Lilly's actions on Aug. 5. Earlier, Denmark's drug regulatory board had restricted use of the drug, primarily to hospitals.

Following U.S. approval of the drug in April, a number of deaths from liver and kidney failure were reported in the United Kingdom. All were among elderly persons who had received the highest dosage (600 milligrams). The British registry of adverse effects subsequently reported many more deaths of persons who had taken benoxaprofen, of which a substantial number were due to gastrointestinal hemorrhage or perforated ulcers. In the United States, 11 deaths associated with the drug were being investigated by the Food and Drug Administration.

In response to reports that mistakenly linked the controversy surrounding Oraflex with FDA's current efforts to improve the drug approval process, FDA noted that the approval time for this drug (28 months) was actually longer than the average approval time for most drugs (24 months). In addition, the agency classified Oraflex as a "C" type drug (having little or no therapeutic value over existing arthritis drugs) and did not target the chemical for priority review.

Under FDA's drug classification system, drugs designated "A" (offering important therapeutic gain) or "B" (offering modest therapeutic gain) take precedence over other drug applications not offering a therapeutic advance. In 1981 the average time for approval of "A" or "B" drugs was 10 months (see "Providing a Breakthrough for Drugs With Promise" in the July-August 1979 *FDA Consumer*).

TENS

by Marti Asper

Thoreau's line about the mass of people leading "lives of quiet desperation" might best describe how it feels to live with chronic pain. Whether sharp, dull, aching or throbbing, chronic pain is still there.

Many people can't get relief from the usual medical remedies—drugs and surgery. Often they are told they must learn to live with their pain. For them, another form of treatment, electrical stimulation, may be helpful.

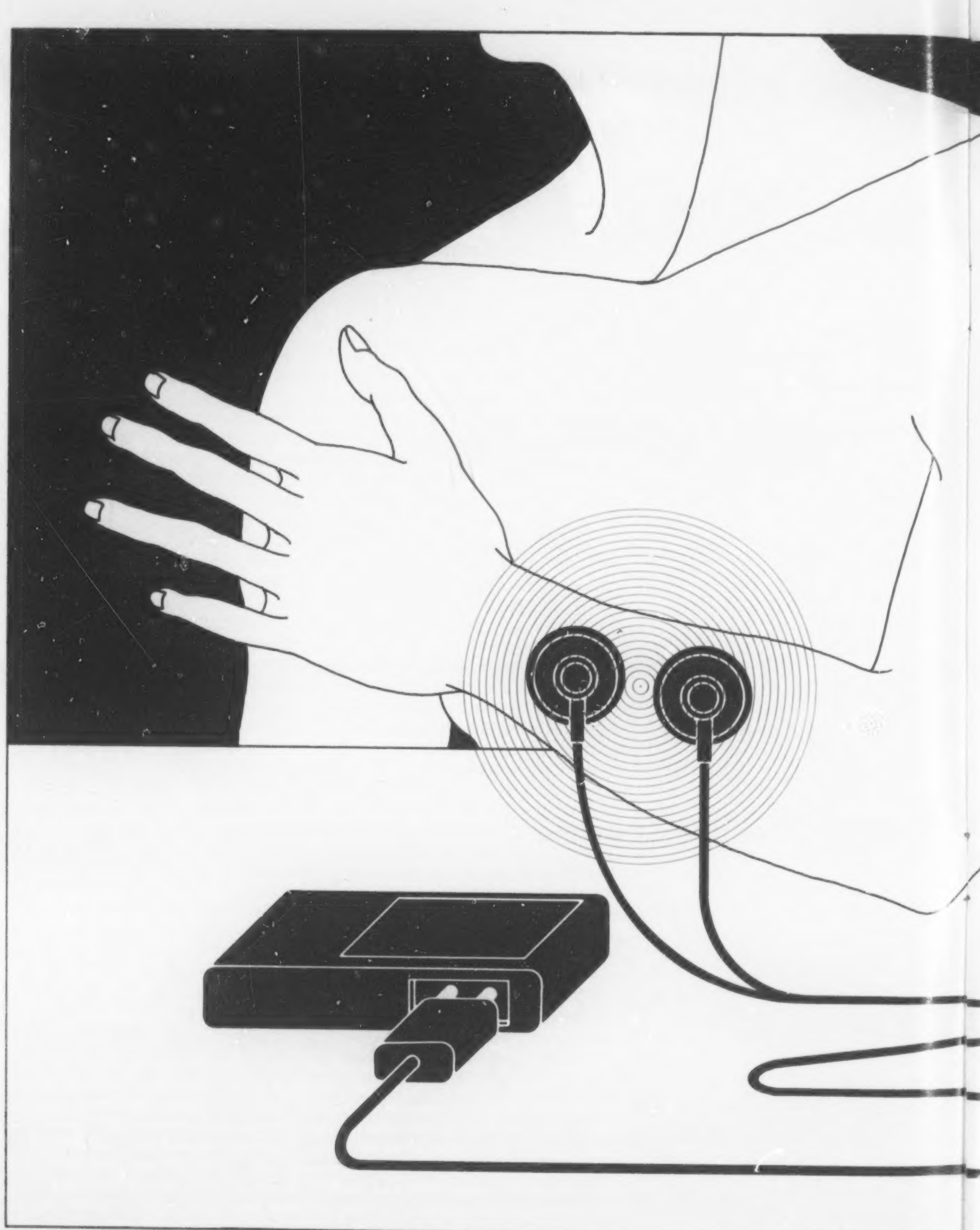
This type of treatment is called transcutaneous electrical nerve stimulation or TENS. The nerve is stimulated transcutaneously (through the skin)—thus, the name.

About 40 brands of TENS devices are on the market with claims of providing some pain relief. Typically, a TENS device consists of a small battery-powered generator about the size of a deck of playing cards, small enough to be carried by hand or worn on a belt clip. Wire leads run from the generator to a pair of electrodes about the size of half dollars. The electrodes, coated with a conductive gel, are placed either directly on or adjacent to the area of pain. When the generator is turned on, pulsating current passes through this area and deadens or alleviates certain kinds of pain. The patient may feel nothing or just a slight tingling at the point of contact, and relief can last hours or days after treatment. In general, TENS devices must be used continuously for chronic pain, but they are also effective for treating some acute pain. The devices sell for $500 to $600 and are available only by prescription.

The knowledge that an electrical charge can dull a nerve is not new. Aristotle noted the ray fish narcotizes its victims by overpowering them with shock. In the time of the Roman Empire, Scribonius Largus, court physician to the Emperor Claudius, experimented with the same fish to relieve headaches.

Medical application of electricity in the United States began in the mid-1700s when Benjamin Franklin opened a Philadelphia clinic to practice "Franklinism," the treatment of paralysis by using mild electric shock. Numerous textbooks and articles on the subject were published a century ago, but the practice waned around 1900, apparently because the instruments were crude and less than effective. Most early applications of electrical stimulation for a variety of disorders were considered quackery. But by the mid-1960s, after further research on electricity and pain, the medical community had renewed its interest in TENS devices for the relief of pain.

TENS works in some individuals and not others and why this is so is a mystery. Dr. Donlin Long, professor and chairman of the Department of Neurosur-



Long said that patients with chronic low back pain, phantom limb pain (an imagined sensation that an amputated limb is still there and hurts) and osteoarthritis (the "wear and tear" form of arthritis) experienced the best relief. TENS was adjudged less successful in treating cancer pain or pain caused by abnormalities of the nervous system.

In a 1981 survey done for FDA by physical therapists, 82.8 percent of the therapists said TENS was satisfactory in giving their patients relief from chronic pain, while 8.2 percent termed results partially satisfactory. Nine percent said the treatment was unsatisfactory.

Judging by these studies, measuring the effectiveness of TENS devices is not an easy task. One reason is that it is difficult to measure the intensity of pain. Pain is a subjective experience influenced by the psychological state of the patient. Environment also can influence a patient's perception of pain, including domestic and work pressures, cultural customs and economic values.

Also, the TENS effectiveness depends on such factors as the proximity of the pain site to the electrode, wave form, wave duration and current intensity, and therapy time. Often a physician or physical therapist tries a number of body locations and electric current settings before finding the best combination.

Although patient responses may vary, FDA's Advisory Panel on Review of Neurological Devices believes that TENS is "an effective method for the treatment of certain types of pain disorders." Said the panel: "Long-term trials in this country have documented a degree of efficacy which is reasonable and acceptable, particularly in view of the very low potential risk to the patient and the absence of alternate low-risk therapy." Low-risk uses for TENS include alleviating acute postoperative pain and often eliminating or reducing the need for narcotics.

The most common risk to health in the use of TENS devices is the possibility of skin burns if the current is too high or the electrodes are too small. Some people may also experience skin reactions to the electrodes or the electrode gel.

FDA's Bureau of Medical Devices says that TENS devices should not be used by a patient wearing a demand-type cardiac pacemaker and should not be placed on the neck over the carotid sinuses, found on both sides of the neck near the collar bone. The flow of electrical current could interfere with the heart's natural rhythm and cause cardiac arrest. Likewise, pregnant women should shun the devices because safety during pregnancy or delivery has not been established. TENS devices should also be kept away from curious children.

TENS products are Class II medical devices. This means that FDA believes that TENS devices' safety and effectiveness can be assured by a combination of general controls and, if necessary, a mandatory performance standard. A voluntary standard for TENS devices is presently being developed by the American Association for Medical Instrumentation.

Marti Asner is a member of FDA's public affairs staff.

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throughout the world. Pure spirulina is a source of protein and contains a number of vitamins and minerals. However, in the amounts normally consumed when taken according to label directions, the nutrients derived are insignificant. As a food, spirulina can be legally marketed as long as it is labeled accurately and contains no contaminated or adulterated substances.

Claims have been made that phenylalanine, an amino acid found in spirulina (and in most other protein sources), "acts on the brain's appetite center to switch off your hunger pangs." However, an FDA advisory panel reviewing data on phenylalanine in 1979 found no reliable scientific data to demonstrate that it is safe and effective as an appetite suppressant.

Some nutritionists fear that consuming large amounts of spirulina might have an effect similar to that of the liquid protein diets which resulted in heart problems and even death for some dieters. Helene Swenerton, a nutritionist at the University of California's Davis Cooperative Extension, points out that because algae are single-celled organisms, they are rich in nucleic acids providing not only a lot of protein but also large amounts of uric acid, which could result in kidney stones or gout.

Another, more recently introduced "natural" pill is dubbed "Glucomannan." Advertised as the "Weight Loss Secret That's Been In The Orient For Over 500 Years," Glucomannan apparently is chemically processed from the konjac root, which has been used as a food in Japan and other Oriental countries for many years.

A search of both the Japanese and English language medical literature, however, shows no studies of this food as a weight-loss product. The manu-

information to substantiate its claims. According to advertising, Glucomannan "helps transport food through your digestive system faster. . . . As a result, more of the calories you do take in (and you're likely to take in fewer, to begin with) can pass out of your system, still undigested, to help your weight loss along even further."

The manufacturer originally claimed that its pill was a food. When FDA wouldn't accept that claim, the firm maintained that its product was GRAS (generally recognized as safe) because it was commonly used in food prior to 1958.

FDA responded that although konjac tubers have been used as food in the United States since at least 1899, the substance in Glucomannan is a chemically processed extract from konjac tubers. This substance is not GRAS for food use and does not have a history of food use in this country before 1958. (Under the food additive law passed by Congress in 1958, any substance intended for food use has to be either GRAS or permitted under a food additive regulation. Substances commonly used as food prior to 1958 are generally recognized as safe.) FDA said that to be marketed as a food substance, Glucomannan would have to either be affirmed as GRAS or approved as a food additive. Both of these require submission of scientific data to FDA.

In addition to miracle pills with unproven claims, another type of dieter's delusion is still being perpetrated by some diet clinics years after both the FDA and the American Medical Association stated it was useless for weight loss.

This deceptive practice is injection with HCG (human chorionic gonadotropin). HCG is a hormone extracted from urine of pregnant women. It is

certain problems of the male reproductive system and in stimulating ovulation in women who have had difficulty becoming pregnant. No evidence has been presented, however, to substantiate claims for HCG as a weight-loss aid.

An article in *JAMA* (*Journal of the American Medical Association*) in 1974 stated:

"No convincing scientific evidence exists that human chorionic gonadotropin has any pharmacologic effect in weight reduction. Hence, claims to the public that such effects do occur are a misrepresentation of the scientific facts."

FDA requires all labeling and advertising of HCG to state that it has not been demonstrated to be effective in the treatment of obesity. The ads must also state that HCG is not approved by FDA as safe and effective in treatment of obesity or weight control.

Yet the use of HCG for weight loss continues. For instance, advertisements for weight-loss clinics using HCG appeared in the Chicago area in the summer of 1982. The ads included the required disclaimer, but in type much smaller than that used to extol the virtues of the clinics' program.

The pill or shot to enable a person to lose weight without danger and without eating less has not been formulated. And the garment or other device to let one firm up or lose inches without moving a muscle has yet to be invented.

It looks like those who want to be slim will have to resort to those old, unglamorous standbys—eating less and exercising more—to shake those excess pounds.

At least until the next waving of the magic wand.

Judith Willis is editor of FDA's Drug Bulletin, *a periodical for health*

Diabetes Is A Controllable Disease With A Growth Factor

by John M. Couric

Diabetes mellitus—directly affecting more than 10 million Americans and growing at a rate of 6 percent a year—remains a major health problem even though the discovery of insulin 61 years ago enormously reduced its mortality rate.

Before insulin was discovered in 1921 and a way found to produce it from the pancreas of animals, diabetes mellitus—in its more severe form—meant almost certain, quick death.

Today, diabetes is one of the diseases in which accurate diagnosis and a proper medical regimen can make a real difference—in longevity and well being. There still is no cure, the cause is still unknown, the disease remains chronic, and children of diabetic parents are more likely to develop diabetes than those of non-diabetics. Nevertheless, the diabetic today can live a relatively normal, productive life. Early diagnosis and careful control of diabetes can reduce the severity of and delay, or possibly prevent, blindness, loss of limbs and other medical complications associated with the disease.

Exactly what is diabetes mellitus? Also known as sugar diabetes, the disease results from the body's failure to process food for energy. In the healthy person, sugar and starches (carbohydrates) in food are changed by digestive juices into a form of sugar called glucose and then used for heat or energy or stored in a slightly different form for later use.

In the diabetic, however, the body does not process glucose properly. This overloads the kidneys in disposing of the excess, forcing the body to use fats and proteins instead of glucose for energy. All of this is the result of a malfunctioning or non-functioning pancreas, the gland in the abdominal region that secretes hormones to aid in digestion. Insulin, one of these hormones, is necessary for the proper use of glucose. If the pancreas does not produce enough insulin or if other substances prevent insulin from performing its primary function, diabetes results. Injecting the right amount of insulin into the body can set the biological mechanism to working properly again and reduce the sugar in the blood.

There is a belief that diabetes is inherited by a child from a parent, sometimes skipping a generation. But not all cases can be attributed to hereditary factors. Other possible causes include previous severe virus infections, environmental factors and some form of autoimmunity—that is, a condition in which a person develops antibodies against constituents of his own tissues. But scientists have not been able to prove any of these theories. About all that can be said with certainty is that obesity worsens and may even

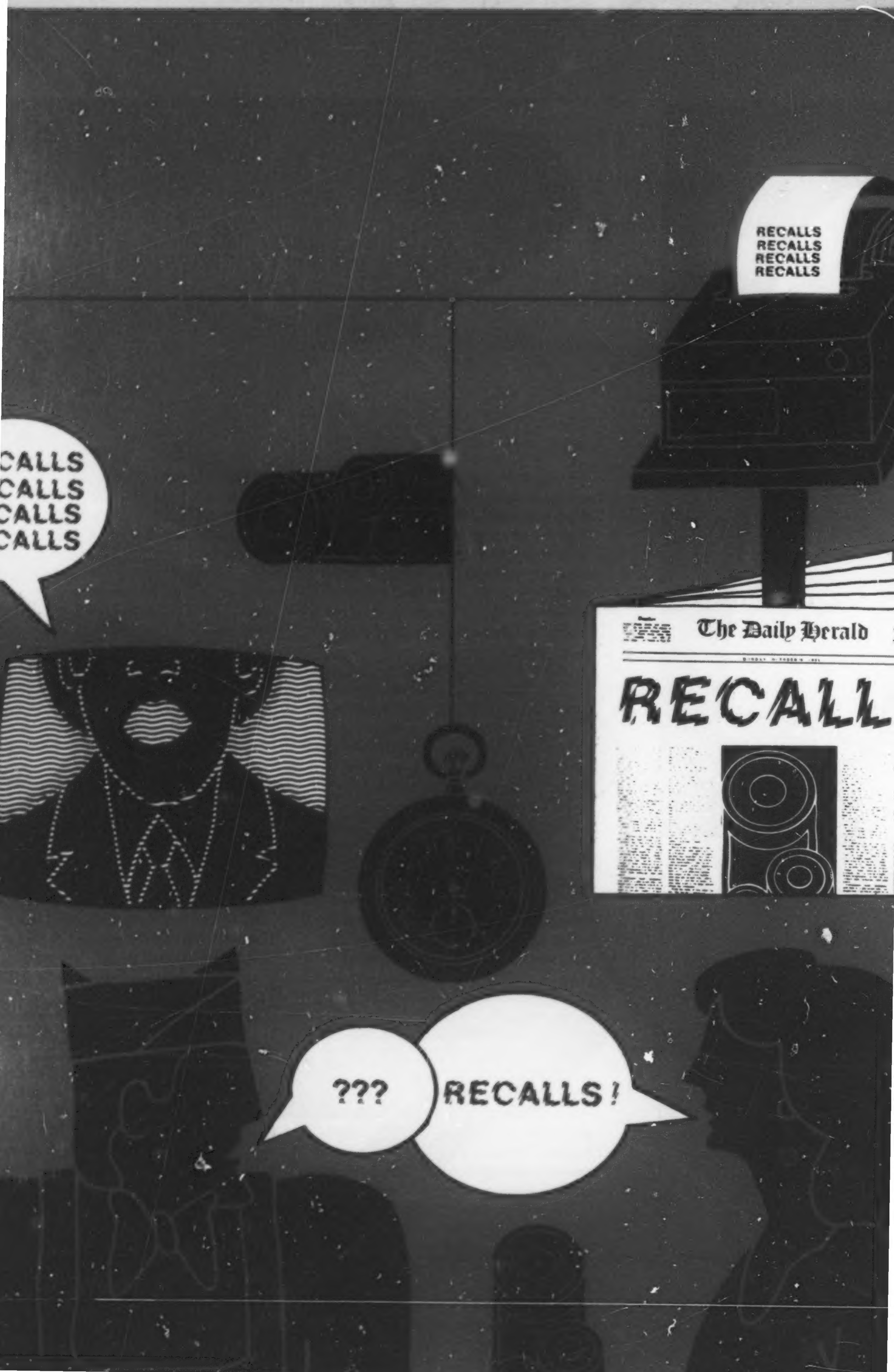
Not all diabetes mellitus cases are alike. There are two major types. Type I formerly was called juvenile-onset, and treatment is dependent upon insulin injections. Type II does not necessarily require insulin treatment and in the past was referred to as maturity-onset diabetes. Type I is more severe. Complications may develop more rapidly and life expectancy may be shortened. Only about 10 percent of diabetes cases are Type I. This form appears very quickly and progresses rapidly, usually in childhood or young adulthood. When it occurs, the patient's pancreas stops producing insulin or produces only a very small amount. Before the discovery of insulin, Type I patients lapsed into a coma and died after a short illness.

The American Diabetes Association, a voluntary, nonprofit health organization, lists these Type I symptoms, which usually occur abruptly:

- Frequent urination accompanied by unusual thirst and excessive drinking of fluids
- Weight loss with easy tiring, weakness, irritability or nausea
- Uncontrollable craving for food, especially sweet foods and candy

Onset is sudden and the need for treatment is urgent or the patient will go into a coma. Insulin, in addition to proper diet, exercise and rest, is always required for treatment.

Type II diabetes is the more common form, usually less sudden and less severe. Generally, it is a disease of middle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Recalls, The Media And Motherhood

by William Grigg

Catching a moment's leisure over a cup of coffee, Mrs. Loving Motherwell glances over her newspaper. War . . . politics . . . taxes and. . . .

What? Little Phil's fruit juice—the one she bought not more than an hour ago—is being recalled by the manufacturer?

Waving the newspaper, Mrs. Motherwell storms back to the grocery. She pokes the paper and the fruit juice in front of the grocer. "What are you trying to do?" she cries. "Kill my Phil?" The grocer bites his tongue. "Of course not," he says, "but I haven't had a recall notice for that product."

"Notice? Shmotice! Can't you read a newspaper?" Mrs. Motherwell snorts. "Idiot!"

Needless to say, neither she nor the grocer is pleased. The mother has been frightened and the grocer has been shouted at, and it wouldn't be human nature for either to think all is well.

Yet, this is the way the system is supposed to work. Indeed, if it's one of the three or four times a year when the Food and Drug Administration issues a press release announcing a food recall, FDA officials have already decided the urgency of the situation justifies scaring Mrs. Motherwell, and others.

There is no faster way to get notice of a recall to the public—and to food markets—than to distribute it to the nation's wire service and have it announced on the 6 p.m. TV news.

Although there are hundreds of recalls each year by drug manufacturers, food distributors and other firms regulated by FDA, there are only a few in which the agency actively seeks newspaper and radio and TV publicity.

FDA classifies these recalls as Class I because they involve a serious threat to life or health, such as a mix-up in a life-saving drug, a dangerous lack of an important nutrient in infant formula, or cans of mushrooms that contain deadly botulinum toxin.

For less serious situations there are Class II and Class III recalls. Class II recalls involve products that may cause temporary or medically reversible adverse health consequences or involve situations where the probability of serious adverse health consequences are remote. In a Class III recall, the use of or exposure to the violative product is not likely to cause adverse health consequences.

By seeking publicity in a Class I recall, FDA not only can spread the word fast but can reach into homes and get consumers to avoid or return already purchased products. This may be inconvenient and even costly to the government and to manufacturers and distributors involved, but in the few cases such an announcement is used, FDA has judged the possible danger to life and health to be worth all the trouble.

Recalls are of two types: those begun by the company on its own and those requested by FDA. When a firm discovers that one of its products is in violation of FDA regulations, that firm may choose to recall the product. Most recalls are this type.

But when a firm fails to recall a defective product on its own, FDA may request it. Such requests are ordinarily made in urgent situations and, generally, FDA will have in hand enough evidence to back up its request with a threat of legal action, such as a seizure of products. This gives the agency's request some muscle, even though FDA has no specific legal authority to *require* a recall.

FDA may portray the alternatives via telephone calls or a visit by a representative from the nearest FDA district office, followed by an electronically delivered letter or telegram.

It remains the firm's responsibility to conduct the recall and to be financially and organizationally prepared to conduct one whenever necessary.

The firm is required to notify each of its affected direct national and foreign accounts promptly about the recall.

The firm should appoint a responsible individual as its recall monitor or coordinator. It is this person's task to coordinate and direct the recall and to establish contact and keep in touch with FDA. The recall coordinator should have company authority to carry the recall to its conclusion.

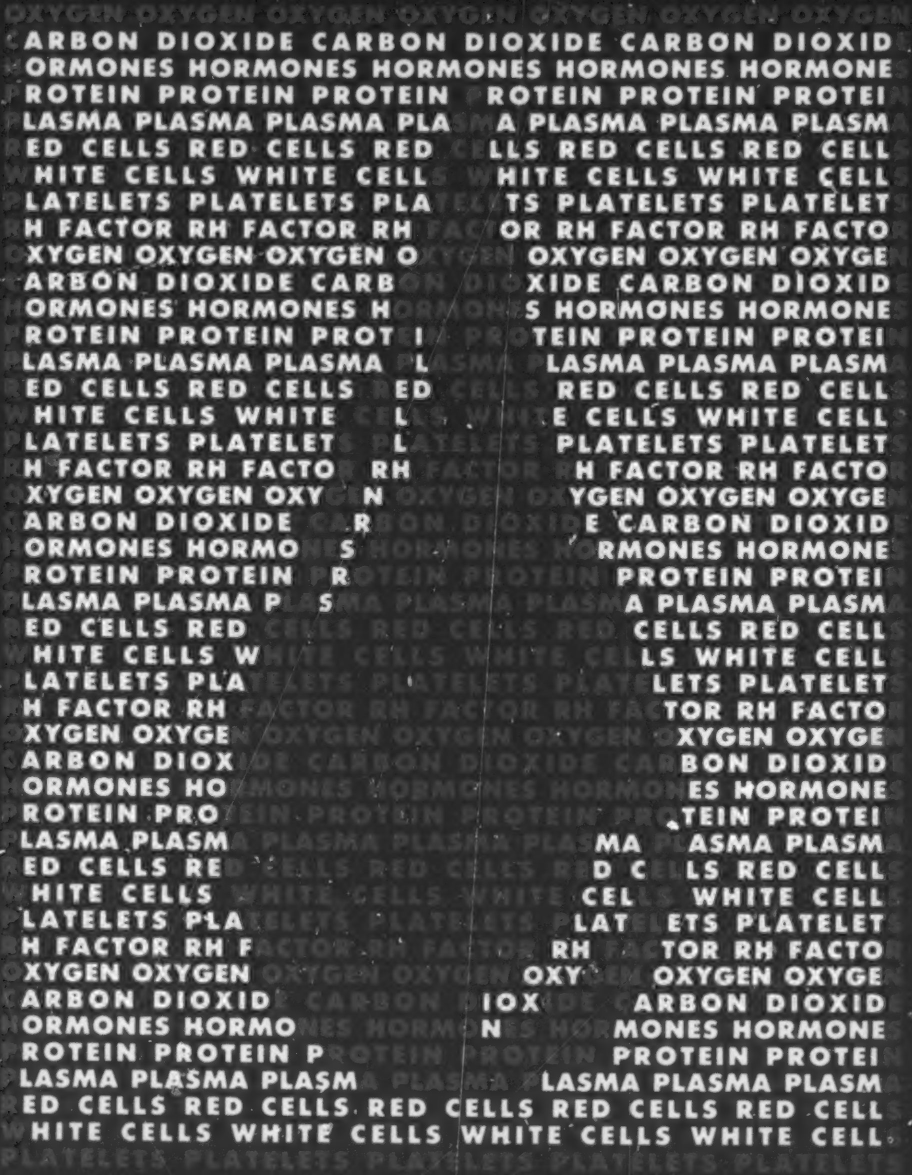
The company should include in its recall plan a way to check the effectiveness or completeness of the recall, asking consignees if they have complied with the recall instructions. In recalls, it's important to quickly relay the recall message and then monitor it to completion. When there is a health hazard, FDA field offices audit the recalls by checking with a fair percentage of the consignees to be sure the product has been removed from the market. The consignees may include the nation's 52,000 drugstores or its 165,000 food retailers—or both.

In a recent infant formula recall, FDA decided to check every one of the consignees. Audit checks sometimes can be done by calling a retailer or wholesaler to be sure he received and acted on the recall notice. The infant formula recall check was so urgent that FDA employees were required to dogsled into remote Alaskan stores where there were no telephones.

When the audits show a product has been completely removed from the market, the recall is terminated.

Attention then can be given to any salvaging and reconditioning operations involving the violative product. A drug that has been improperly labeled can be dangerous but often it can be easily and safely reconditioned just by replacing the label. If a recall was made because a certain number of cans were malformed by a machine that started to function improperly, sometimes the faulty containers can be discovered by inspection and isolated. The others can then be returned to the market.

William Grigg is director of FDA's press relations staff.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Blood: A Fluid You

by Louise Fenn

Blood. A powerful word. You can't say it without seeing the color. Blood is life itself and, despite experiments with liquids that perform some of blood's functions, there is still no substitute for the genuine article. The only source is the human body.

Blood performs a multitude of functions as it travels between the heart and the far-flung outposts of the body. It carries oxygen to the cells and removes carbon dioxide and other waste products. It transports food and water as well as hormones and other substances vital to maintaining health. It carries the cells and proteins that fight infections and protect the body from invaders. And the list could go on.

The fluid part of blood, which transports everything else, is called plasma. It is a solution of proteins and other substances in water and comprises about 55 percent of blood's volume. The other 45 percent consists of red cells, white cells and platelets. The red-colored hemoglobin in red cells enables them to carry oxygen and carbon dioxide. White cells are the body's guardians against invaders, and platelets are essential to clotting and to the repair of injured blood vessels.

The average man has 10 to 12 pints of blood and the average woman eight or nine pints. A healthy adult can easily spare a pint, the approximate amount of a blood donation. The body replaces the lost fluid within a few hours. Red cells are replaced more slowly, but well before a person is eligible to donate again, after a required eight-week wait.

A person may donate plasma much more frequently than whole blood, as often as twice a week. In a process called plasmapheresis, a pint of the donor's blood is removed, the red cells are separated from the plasma, and the cells are then returned to the donor along with enough added saline solution to make up for the lost fluid. The process is repeated to obtain the plasma from two pints of blood.

Since plasmapheresis takes about two hours, plasma centers usually pay their donors to compensate for the time

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Can Bank On

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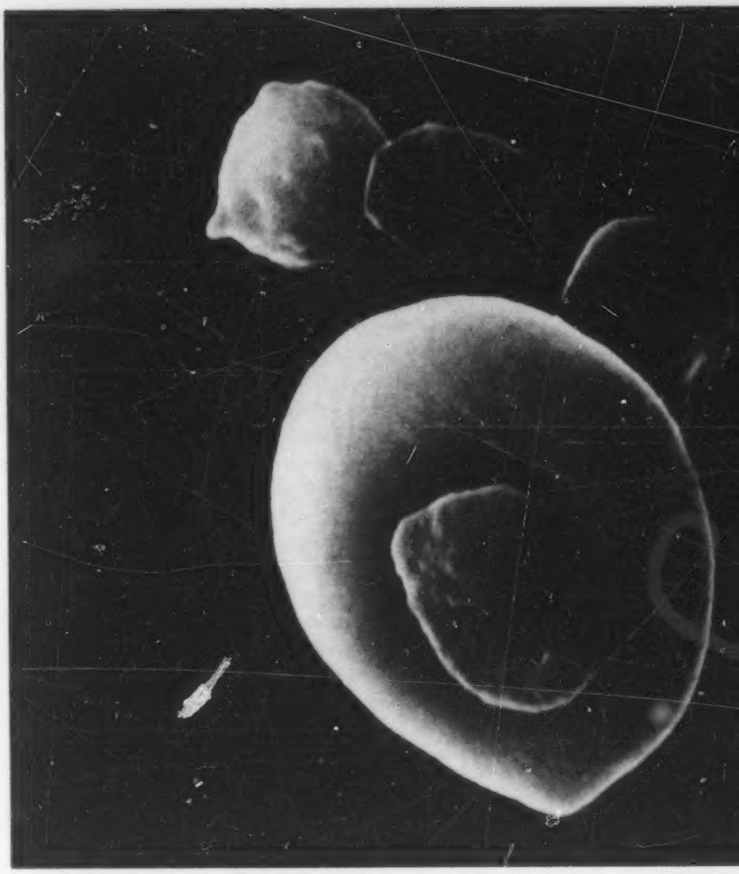
ved. In contrast, over 95 percent of whole blood is
voluntarily. Blood donation takes only about 30 to 40
tes, including a brief medical examination, with less
10 minutes spent actually drawing the blood.
e American Blood Commission estimates that approx-
ly 40 percent of the American population is medically
le to give blood. However, less than 10 percent of
people, or about 4 percent of the total population,
lly donate. In 1980, the most recent year for which
s are available, nearly 11 million units (pints) of
blood were donated.
st blood is not transfused as whole blood but is
ed into its components so that a single unit can benefit
l patients. For example, one unit of whole blood
be divided into red cells for use in a patient with
ia, platelets for a leukemia victim undergoing chemo-
py, and plasma for a trauma patient who needs
a volume restored. In this way, the nearly 11 million
ed units of whole blood in 1980 were converted into
than 14.8 million transfused units. Nowadays, whole
is used in less than one-sixth of all transfusions.
ddition to blood, Americans donate 10 to 11 million
of plasma each year at plasmapheresis centers. This
a is not directly transfused; instead, it is sold to
aceutical manufacturers for processing into essential
al products. Because it is the source of many manu-
ed products, it is called "source" plasma to differen-
from plasma that is transfused ("single donor"
a). Source plasma is broken down by the manufac-
into various proteins, which are then concentrated
ppropriate strengths for different uses. Some of the
products that result are serum albumin (used to treat
and burns), immune globulins (which are rich in
dies and can provide temporary immunity to various
es), and protein clotting factors (used to treat
hilia).
transfusion of blood and its components now

The large doughnut-shaped structure in this scanning electron micrograph (right) is a normal red blood cell, highly magnified. In front of it is a platelet, and three platelets are seen above.

Less than 10 minutes is spent drawing approximately a pint of blood from Jean Fair, a regular donor at a suburban Washington, D.C., Blood Bank (page 13, top left).

The finger prick has been updated: now one quick punch and it's all over, and painless. A few drops of blood must be tested for red cell content and hemoglobin level before the donor can be accepted (page 13, top right).

This full blood collection bag contains anticoagulant solution and 475 grams of the donor's blood. The next step is determination of the blood group and type, which is done as soon as possible and the bag so marked (page 13, bottom).



happens some 37,000 times a day in the United States. However, until the beginning of this century transfusions were seldom performed because of the risk of unpredictable and often fatal reactions. In 1900, scientists discovered the existence of three blood groups among the population and learned that severe transfusion reactions could occur when patients received blood from groups other than their own. A fourth blood group was discovered two years later. Now all blood is classified into four major groups: A, B, O and AB.

When a person receives blood from the wrong group, naturally occurring antibodies in his or her plasma may attack the transfused blood. This can cause the transfused red cells to rupture and release their hemoglobin, with resulting shock, kidney failure and even death (although prompt treatment rescues most victims). While incompatibility between red cells causes some problems in about 1 in 6,000 transfusions of whole blood or red cells, life-threatening reactions are much less common. Every unit of donated blood is tested twice to determine its group, and the blood is again tested to assure that it is compatible with the recipient's before transfusion.

Two more major discoveries occurred before blood transfusions became safe and commonly accepted. In 1914, just in time for World War I, a non-toxic anticoagulant called sodium citrate came into use which prevented blood from clotting when removed from the body. Blood could be kept under refrigeration for three or four days before deteriorating. Storage time for whole blood and red cells is now up to 35 days because of better anticoagulant-pres and plastic equipment that permits sterile preparat individual blood components. Different storage te make the most of the various components. For ins plasma and certain protein-clotting factors can be years if frozen. Until recently, fragile platelets coul stored only three days; however, new plastic storag approved by the Food and Drug Administration i extended this time to five days.

In 1940 scientists discovered the Rh factor, nam the Rhesus monkeys that were used in experiment to its disclosure. In America, 85 percent of the pop has blood that contains the Rh factor. Their blood Rh positive. Blood without the factor is called Rh

The Rh factor is significant because the Rh type always compatible. People with Rh-negative blood develop antibodies to the Rh factor if they receive fusion of Rh-positive blood. Once the antibodies the Rh-negative individual can never again receive positive blood because the antibodies will destroy

This fact is especially important to a woman wi negative blood who has an Rh-positive baby (whi happen if the father has Rh-positive blood). Since the baby's blood mixes with hers during pregnanc delivery, she may develop anti-Rh antibodies. The has a second baby with Rh-positive blood, her ant could cross the placenta and attack the red cells o child. The baby may be severely affected and may before birth. An affected newborn may require an

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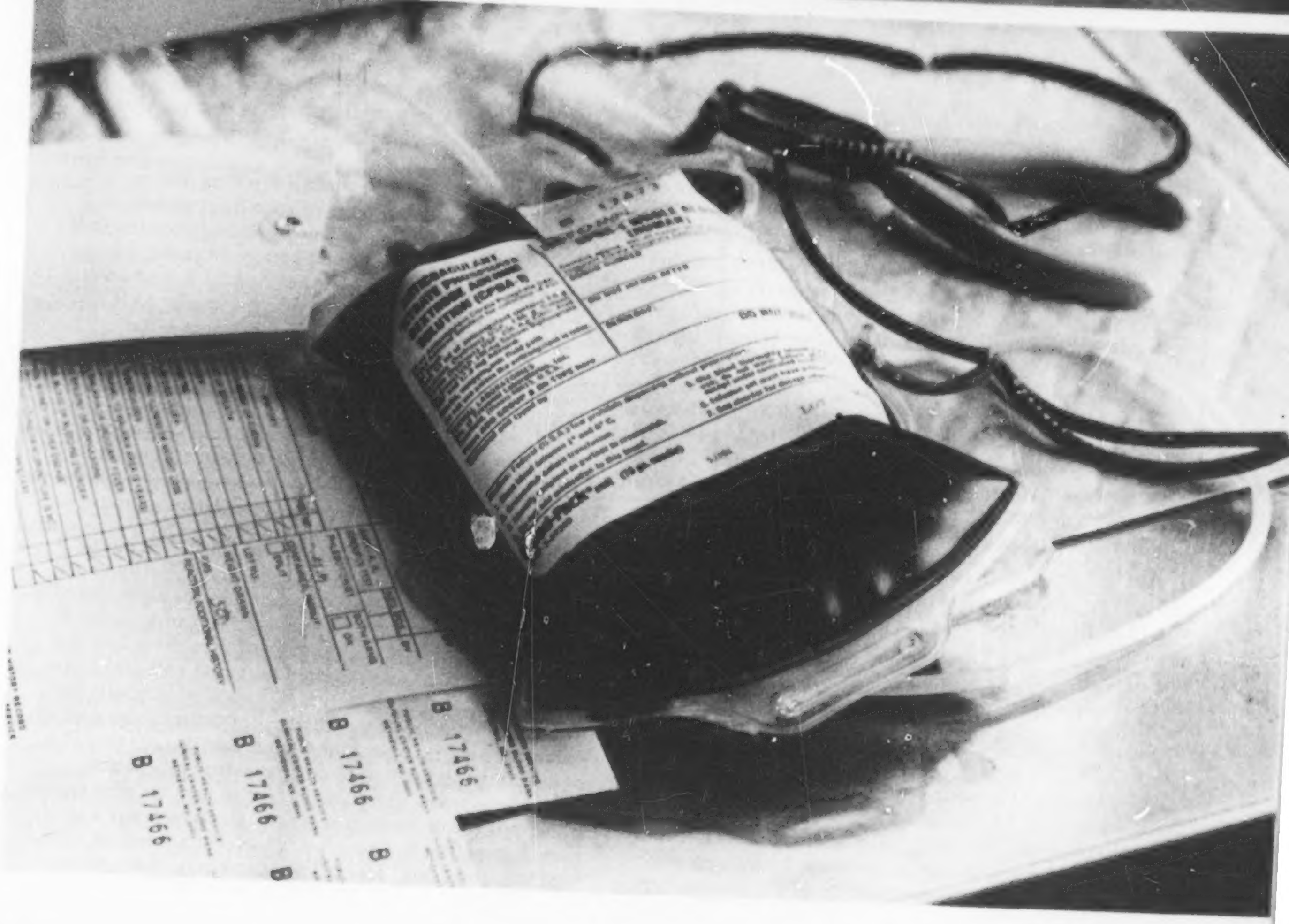
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Blood Component Therapy

CELLULAR ELEMENTS		PLASMA	
Red Cells	Used for treatment of anemia. Also can serve for majority of blood transfusions.	**Plasma**	Historically, fresh frozen and single donor plasma have been used to restore plasma volume and to control bleeding.
White Cells	Used for combating infections. Clinical use experimental at present.	**Cryoprecipitated Antihemophilic Factor**	Prepared from fresh frozen plasma. Contains clotting factor (factor VIII) therapeutic for hemophilia A.
Platelets	Used in cancer patients, especially those with leukemia, to reverse low platelet count due to chemotherapy.	**Plasma Proteins**	
		Serum Albumin	Used to restore blood volume in case of trauma.
		Immune Globulins	Contain antibodies against diseases. Immune serum globulin is used for prevention of hepatitis A and measles and also for treatment of immunoglobulin deficiencies. Specific immune globulins are used for prevention of hepatitis B, rabies, tetanus and chicken pox in immunosuppressed patients. Also includes Rh immune globulin.
		Clotting Factor Concentrates	Used to control bleeding due to deficiencies of specific coagulation factors: antihemophilic factor (factor VIII) for hemophilia A; factor IX complex for hemophilia B; and anti-inhibitor coagulant complex (AICC) for hemophilia A patients with antibodies to factor VIII.

"exchange" transfusion shortly after birth to remove the Rh-positive blood which is being destroyed and replace it with fresh Rh-negative blood. Fortunately, it is possible to prevent a woman with Rh-negative blood from developing anti-Rh antibodies by giving her an injection of a substance called Rh immune globulin after the birth of each Rh-positive child.

One problem involving blood transfusion is not yet completely solved. A viral infection of the liver called hepatitis can be transmitted in whole blood, plasma and some plasma products. The infection can be mild and virtually without symptoms, but more serious infections can lead to chronic liver disease, including cirrhosis. There also has been evidence linking at least one type of the disease, hepatitis B, with an increased risk of liver cancer. Hepatitis B strikes an estimated 200,000 Americans, primarily young adults, each year—with about a tenth of the cases linked to transfusions. Of the unfortunate 1 percent of hepatitis B victims whose disease is extremely severe, about half die.

Since 1972 FDA has required all blood and blood products to be tested for hepatitis B. Labels of products for transfusion must indicate whether they come from paid or volunteer donors, since blood from paid donors carries a significantly higher risk of post-transfusion hepatitis.

On the average, about 10 percent of persons who receive transfusions will develop hepatitis. However, only 1 in 10 cases is hepatitis B. The other 90 percent are non-A, non-B hepatitis, so-called because symptoms exist that are not

Percentage of People in the United States With Different Blood Groups and Rh Types

ABO Group and Rh Type	How Many Have It	Frequency
O Positive	1 person in 3	37.4%
O Negative	1 person in 15	6.6%
A Positive	1 person in 3	35.7%
A Negative	1 person in 16	6.3%
B Positive	1 person in 12	8.5%
B Negative	1 person in 67	1.5%
AB Positive	1 person in 29	3.4%
AB Negative	1 person in 167	0.6%

caused by the hepatitis A or B viruses. (Hepatitis A is not carried by blood.) There is no specific test to detect whether blood is carrying non-A, non-B hepatitis. About 200,000 cases of post-transfusion hepatitis occur annually in the United States.

A vaccine to prevent hepatitis B was approved by FDA in 1981 and recommended for use in high-risk groups, but no such preventive exists for non-A, non-B hepatitis. Among the people at highest risk for hepatitis B are health-care workers, patients and staff at institutions for the mentally retarded, hemodialysis patients, homosexually active males, illicit injectable drug users, recipients of certain blood products (e.g., hemophiliacs), household and sexual contacts of hepatitis B carriers, immigrants from high-risk areas, and prison inmates.

In addition to hepatitis B testing, FDA has other requirements aimed at assuring the safety of blood and blood products and protecting consumers. Blood establishments are required to register with FDA, and those that ship products in interstate commerce must also be licensed. In 1975 FDA established Good Manufacturing Practice regulations for blood establishments. These regulations cover personnel, facilities and equipment, quality control, recordkeeping, and reporting of adverse reactions to FDA. Specific standards also exist for individual blood products.

A little over 2,000 blood establishments are registered with FDA. Licensed hospital and community blood banks, donor and distribution centers account for about 650 of this total. Approximately another 1,000 such firms operate only within their state borders. Also among the registered firms are some 350 licensed plasmapheresis centers, as well as about 50 diagnostic product manufacturers, laboratories, producers of plasma derivatives and other firms.

Each registered blood firm is inspected at least once every two years by FDA field investigators. The agency can suspend or revoke the license of a firm that does not fulfill its responsibility to protect donors and the blood supply. Other legal action, including prosecution, is also an option. However, such measures are seldom required.

One fairly recent medical innovation concerning blood has been the increasing focus on a blood treatment method called apheresis. It has been used experimentally to treat myasthenia gravis, systemic lupus erythematosus and other disorders that are linked to abnormalities in the immune system. During apheresis, blood flows from the patient to a machine where certain components thought to be connected with the disease are separated off. The remaining components are then returned to the patient.

An example is plasmapheresis for patients with myasthenia gravis. Since some of the patient's symptoms are related to antibodies in the plasma that attack the patient's own body, extracting the plasma and replacing it with plasma substitutes, such as serum albumin, may relieve symptoms until the antibody builds up again.

One type of apheresis device uses a centrifuge to separate the heavier parts of the blood from the lighter ones. In 1981 FDA approved a plasmapheresis device that employs a membrane filter to extract the plasma from the cellular elements of the blood. However, much research is still needed on the effectiveness of apheresis—sometimes called a modern version of bloodletting—in the treatment of various diseases.

Studies are also under way for testing a synthetic blood supplement made from oxygen-carrying compounds called perfluorocarbons. First suggested by American scientists in the mid-1960s, perfluorocarbons were produced in Japan in 1979. There they have been transfused into numerous patients at times when matching blood was not immediately available. In the United States the perfluorocarbon substance is an investigational drug being used by selected investigators under very carefully controlled conditions. Patients treated include those with severe anemia whose religion may forbid blood transfusions.

In cases of severe blood loss, perfluorocarbons can be temporarily used to transport oxygen through the body. They do not have to be matched with a patient's blood group or Rh type. However, perfluorocarbons cannot perform blood's other important functions, such as clotting, carrying nutrients and other substances, and fighting infection. Therefore, they should not be thought of as a blood substitute but rather as an alternate method of delivering oxygen to the body.

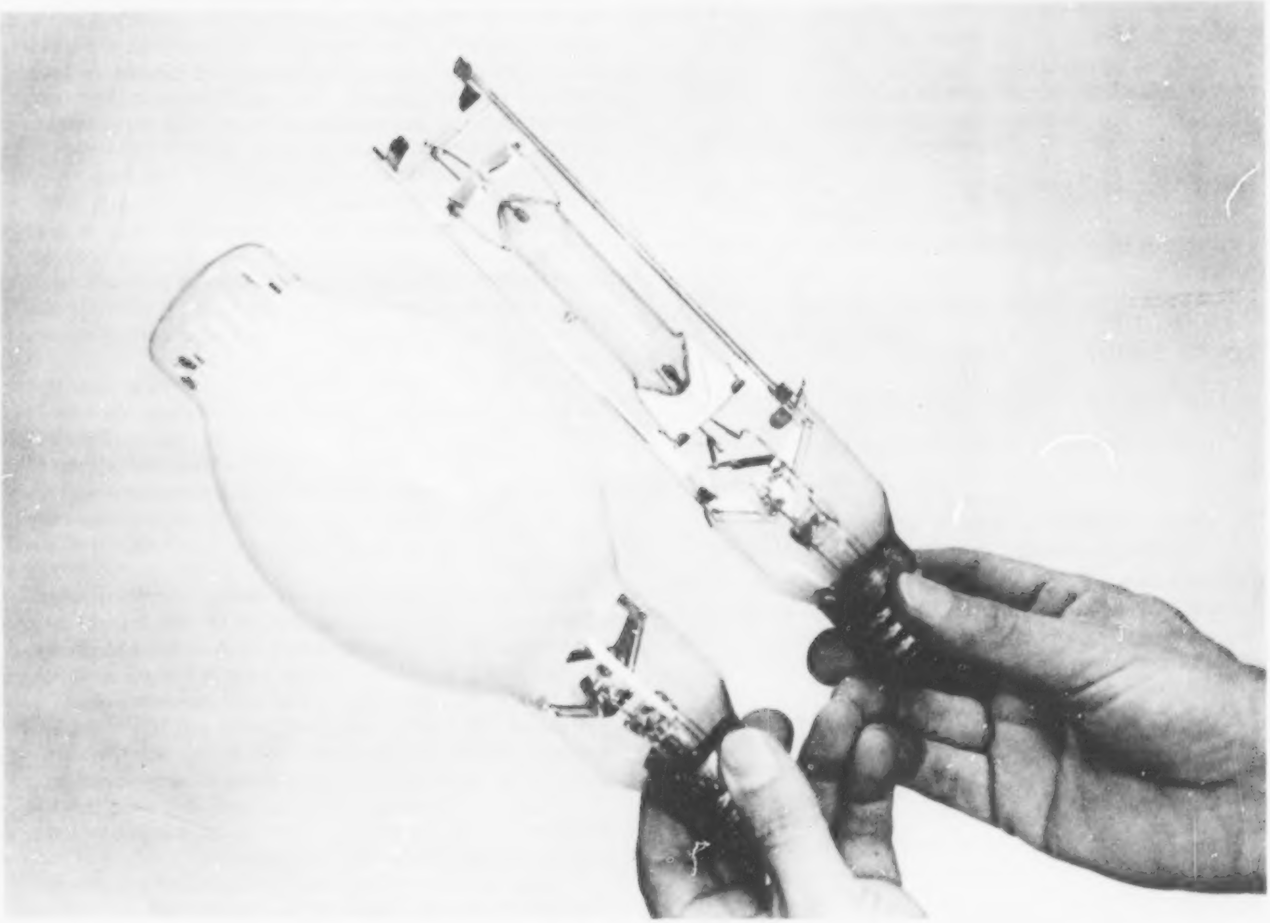
There is also intensive research on a chemically modified hemoglobin prepared from blood. It can be stored in freeze-dried form at room temperature, reconstituted and administered without concern for blood group and type. Someday such a product might be used when red cells are available, as during wartime combat or a mass emergency. Studies on humans are yet to be done with the substance.

As it stands, people who need blood still have to count on their friendly neighborhood blood bank.

Louise Fenner is a member of FDA's public affairs staff.

When A Broken Lamp Burns

by William B. Knight



The mercury vapor lamp at top is the same kind as the one at bottom, but the coated glass envelope has been broken off. Even though the envelope is broken, the bulb can continue to operate, giving off harmful ultraviolet radiation.

A rough game of basketball is usually associated with a few bruises and some general aches and pains, but not with red eyes, swollen eyelids or sunburn-like symptoms. Yet those latter symptoms were suffered by 26 persons when the cover of a mercury vapor lamp broke but the lamp kept burning in a New Jersey community center gymnasium. When FDA scientists made measurements on a broken lamp identical to the one in New Jersey, they found ultraviolet radiation emissions over a hundred times in excess of recommended safe levels.

For reasons of economy, those bright bluish-white mercury vapor lights are being used more and more to light large areas such as gyms, shopping centers, parking lots and streets. The lifetime of a mercury vapor lamp is many times longer than that of a conventional tungsten lamp and, for a given amount of electrical power, the mercury vapor lamp provides much more light than a tungsten lamp.

Mercury vapor lamps differ from tungsten filament lamps in that the mercury vapor lamp uses an electric arc produced within a quartz tube in the middle of the lamp instead of the heated metal filament of a tungsten lamp. High-intensity ultraviolet radiation, as well as visible light, is emitted by the mercury vapor in this tube. A borosilicate glass envelope surrounds the quartz tube. When intact, this envelope prevents the shortwave component of the ultraviolet radiation from leaving the lamp.

But if any or all of the envelope is broken off and the lamp continues to operate, the problems with ultraviolet radiation begin. Naturally occurring ultraviolet radiation produced by the sun causes skin tanning and, if overexposure occurs, burning. The shortwave ultraviolet radiation that escapes from the broken lamps can cause sunburn and photokeratitis (an inflammation of part of the eye that causes a painful, gritty sensation). The severity of the effects depends on the distance from the lamp and on the length of exposure, as well as the individual's sensitivity to ultraviolet radiation. Very long exposures may result in permanent damage to the skin or eyes.

Broken mercury vapor lamps represent an insidious hazard for two reasons. First, a person may not be aware that he or she is being exposed to the invisible ultraviolet radiation, or know of the possible results of such exposure. And, to make matters worse, the symptoms in most cases will not appear until several hours after the exposure.

The New Jersey case described above was not an isolated one. Since 1969, 42 incidents of ultraviolet radiation injury involving about 700 persons have been reported to the Food and Drug Administration. Other incidents may have occurred that were either not reported or not diagnosed as related to ultraviolet radiation.

In an attempt to prevent future injuries, FDA's Bureau of Radiological Health has taken steps to make mercury vapor lamps safer for the consumer. With responsibility for the safety of light products, the bureau evaluates optical emissions and develops and enforces standards.

Standards for mercury vapor lamps went into effect in March 1980. Lamps designated as "self-extinguishing" (those that automatically go out when the glass envelope is broken) must be clearly marked with the letter "T," and the electric arc must extinguish within 15 minutes of breakage of the protective glass envelope. In addition, the standard specifies that those lamps that do not have the self-extinguishing feature must be clearly marked with the letter "R," and that packaging and advertisements for these lamps must display appropriate warnings relating to potential ultraviolet radiation hazards. For both lamp types, instructions for safe use must accompany each lamp.

The more expensive, self-extinguishing lamps were not made mandatory because in some situations the cheaper models do not pose a danger. In some

remote locations such as ski slopes a person would be unlikely to remain exposed to a lamp long enough for it to constitute a hazard. Also, in many such instances the lamps are placed considerably farther from people than lamps used indoors.

Still another protective method is a protective shield made of a special glass or hard plastic and designed to fit over the lamp reflector. Such shields absorb ultraviolet radiation and help protect the lamp from flying objects.

Consumers can take some steps to reduce the possibility of ultraviolet exposure from a broken mercury vapor lamp. Areas with broken or suspected broken lamp envelopes should be avoided. Further, a responsible person should be alerted to the potential problem so that the lamp can be turned off and checked or replaced if needed.

Should skin burns and eye irritation develop following exposure to ultraviolet radiation from a broken mercury vapor lamp, a physician should be consulted and informed of the ultraviolet radiation exposure. Also, the incident should be reported to the state health department and FDA.

The person responsible for the lamp

guidelines for use, check the lamp regularly for breakage when it is turned off, and replace broken lamps only when the current is turned off.

In recent years, orange-glowing sodium vapor lamps have appeared on roadways and in large buildings. These are another member of the family of high-intensity discharge lamps. However, sodium vapor lamps produce much less ultraviolet radiation, and the risk of acute eye or skin injury from intact or broken lamps is not significant.

Other high-intensity lamps include metal halide lamps (sometimes substituted for mercury vapor lamps) and sunlamps. Metal halide lamps are so close in nature to the mercury vapor lamps that the mercury vapor performance standard also is applicable to them. Sunlamps, which are purposely designed to emit ultraviolet radiation, have great potential for causing injury even when intact. FDA has a separate performance standard for sunlamps. Even so, it remains up to the user to exercise care and good judgment in using these lamps.

Some uses of mercury vapor lamps carry more potential risk to more people than the ordinary if a bulb should become defective and begin emitting harmful amounts of ultraviolet radiation. One such use is in gymnasiums, where both players and fans may receive harmful doses should the bulb defect go unnoticed.

William B. Knight is an optical engineer with FDA's Bureau of Radiologi-

About Body Wraps, Pills And Other Magic Wands For Losing Weight

by Judith Willis

Overweight and out of shape?
Want to lose pounds withou
dieting and eliminate inches witho
exerting any effort?

So do millions of Americans w
believe that somehow, as if by wa
a magic wand, they will be thin a
firm. Unwilling or unable to lose
weight through diet and exercise,
turn to weight-loss gimmicks ran
from pills that supposedly let the
unlimited pasta to rubber suits th
make them sweat while they sleep

Most current diet gimmicks see
fall into two categories: (1) custo
garments or body wraps that clai
"melt" fat away in a short time, a
(2) pills that supposedly curb app
without side effects, or allow diet
eat as much as—or more than—
normal and still lose weight. The
are usually touted as the product
some previously undiscovered pr

Who can blame the fretfully fla
for being lured by the promise of
ing inches without doing anythin
more strenuous than popping a p
wrapping up the offending flesh?
can resist ads for body wraps tha
promise "to burn away fat even w
you sleep," to "lose 4-6 inches the
day"?

Some of the plastic or rubber g
ments are worn around the waist,
some cover the waist, hips and th
and others cover nearly the entire
body.

Some are to be worn while car
out routine activities, others whil
exercising, and some while sleepi
One is inflated with air from a va
cleaner. Another uses an electric
dryer to blow in warm air. Some
used after a cream, gel or lotion i
applied or after the wrap is soake
a solution.

The Food and Drug Administr
has investigated a number of thes
products and has taken action ag
several promoters of wrapping de
and latex exercise or sweat suits f

making unsubstantiated medical or therapeutic claims.

The garments and wraps, with or without lotions and creams, reduce body dimensions by removing fluids. Most medical experts agree that such treatment will cause a loss of inches and perhaps pounds due to profuse perspiration, but the reductions are temporary. The fluid is soon replaced by drinking or eating. But rapid and excessive fluid loss is potentially dangerous because it can bring on severe dehydration and can upset the balance of important electrolytes in the body.

Wraps have no effect on fat deposits and will not dissolve fat, even temporarily. Fat is not broken down by perspiration. It is gotten rid of only when fewer calories are consumed than are needed to meet the body's energy requirements.

The latest twist in the body wrap bonanza is a product called La Creme, a cream to be applied to parts of the body where loss of inches is desired. La Creme differs from other wrap products in that the wrap is not sold along with it. Rather, consumers may choose their own wraps from among the plastic products normally used to wrap food. La Creme is applied and then six or seven layers of the plastic wrap are wound around the creamed area.

A leaflet for the product claims: "Lose up to two inches from those problem areas in just one hour." An advertisement adds, "Its gentle warmth penetrates into your skin and helps melt fatty deposits." But, as with other wraps, any weight or inches that disappear are lost from perspiration. (See "Fat Won't Melt," an Update in the November 1981 *FDA Consumer*.)

Promotional literature distributed to retail outlets, such as department stores and specialty salons, claimed that FDA had approved or classified La Creme as a skin toner, tightener and smoother. In truth, FDA had never been given an opportunity to evaluate the product and had no idea what it contained.

FDA advised a distributor of La Creme that, based on the product's labeling, it should be regulated as a drug because it claimed to alter the size, shape or conformity of the body—a drug function as defined by the federal Food, Drug, and Cosmetic Act. When the distributor contended that La Creme was a cosmetic and therefore not subject to safety and efficacy requirements, FDA replied that claims of even temporary reduction of body measurements were not appropriate to a cosmetic.

The company has not replied to FDA's comments. In the meantime, many of the department stores that carried La Creme have stopped selling it.

In resorting to magical slimming items, the weight conscious are often either taking risks with untested products that may alter the body's functioning or being duped by products that have no more effect than a placebo.(Only two drugs—phenylpropanolamine and benzocaine, along with caffeine—should be used in non-prescription diet aids, according to an FDA advisory panel. Those recommendations have not been acted on by the agency.)

Yet, the marketing of untested diet aids persists. They appear on the market without FDA approval because manufacturers often contend that their product is a food and thus not subject to premarket approval from FDA as a drug would be.

Often a product does not come to FDA's attention until it has been used by a substantial number of persons, some of whom may be harmed by it.

Starch blockers are an example of a product sold as a food but considered by FDA to be a drug. Advertised and sold nationwide, starch blockers allegedly block or impede starch digestion and thus help in weight control and weight reduction. One manufacturer touted the product as "a revolutionary new concept in natural weight control." Print and TV ads claimed people taking starch blocker pills could eat up to 600 calories a day of foods such as bread, potatoes and pasta without absorbing the calories.

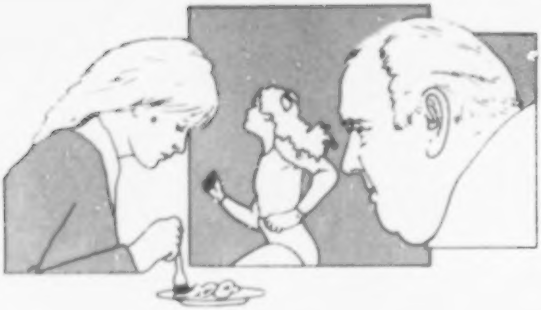
Manufacturers did not seek FDA approval before putting starch blockers on the market. They claimed the product, prepared from raw beans, was a "special dietary food" instead of a drug.

FDA disagreed. The agency asked the manufacturers to discontinue marketing starch blockers until scientific testing could confirm their safety and efficacy as drugs.

Users of these products have complained to FDA of nausea, vomiting, diarrhea and stomach pains. The pills are considered to be particularly hazardous to diabetics, who may rely on their purported carbohydrate-blocking effect to calculate their diets.

Although these products are made from a food substance, FDA considers them to be drugs because of the claim that they control or reduce weight by blocking or interfering with digestion. According to the starch blocker theory, the pills contain a substance that inhibits the activity of the enzyme amylase, which digests carbohydrates. This constitutes a drug action that may interfere with the body's normal metabolism. Under the FDC Act, a substance that is offered for a non-food purpose and that affects a function of the body is a drug, not a food, even if it is derived from a vegetable.

Another natural substance promoted as a weight-loss wonder is spirulina. It is sold as a food or food supplement in the form of a dark green powder or pill in many health food stores. Spirulina is one of about 1,500 known species of blue-green algae that grow in brackish ponds and lakes in mild and hot climates



less insulin and at a slower rate. Common Type II diabetes symptoms include:

- Any Type I symptom
- Frequent infections of the skin, gums or urinary system
- Unusual changed or blurred vision
- Pain or cramps in legs, feet and fingers
- Slow healing of cuts and bruises
- Intense itching
- Drowsiness

Only a physician can be sure that the patient has the disease, by using one or more laboratory procedures, including a urine test, a simple blood test and a blood glucose (sugar) tolerance test. A blood sugar test is useful for checking older people who do not have the classic symptoms but may just not feel well.

Although medical science does not know the basic cause of diabetes, one undisputed trigger for the onset of Type II is F-A-T. Weight loss through diet is mandatory for the overweight diabetic. If proper weight is maintained, many diabetics over 40 will not need additional treatment. If they do need it, the physician will combine medication—insulin injections or oral drugs—with diet. In a diabetic diet, the number of calories must be constant. Concentrated sugars such as those found in candies, baked goods and soft drinks are prohibited because the insulin in the diabetic cannot burn them fast enough.

Exercise and proper rest also are important for all diabetics. Exercise helps burn up food and takes some of the demand for insulin off the pancreas and also assists in maintaining proper weight. Necessary rest varies with the individual, but fatigue can affect body efficiency.

A diabetic's meals, exercise, medication and rest should follow a regular schedule. Insulin shock due to hypoglycemia (too little sugar in the blood) may result if the diet-exercise-insulin regimen is disrupted. Not eating enough, exercising too strenuously or taking too much insulin can upset the balance.

Wide swings in blood sugar levels may occur when the diet-exercise-insulin balance is disrupted. Among the symptoms of too little sugar in the blood are tremors, hunger, sweating, headache, nausea, blurred vision and—if untreated—loss of consciousness. The diabetic can get prompt relief by ingesting candy, orange juice or some other sugary food or beverage. In addition, the patient's physician should be contacted immediately.

Too much sugar in the blood (hyperglycemia) can result in diabetic coma. The sugar buildup can be attributed to insufficient insulin or failure to follow the proper diet. The patient's symptoms can include nausea, drowsiness, extreme thirst, headache, blurred vision, abdominal pains
and rapid breathing. If the condition is not treate
ing the blood sugar level with insulin, loss of con
and coma will result.

Insulin cannot be taken orally but must be inj
the skin. The digestive juices apparently destroy t
mone. Other drugs, taken by mouth, have been a
for the treatment of adult-onset diabetes since 19
drugs, which come in tablet or capsule form, are
lower the blood sugar level by stimulating the pr
of insulin in the pancreas.

The National Institute of Arthritis, Metabolis
Digestive Diseases says that, while these drugs ha
widely used, a recent 10-year study of their effect
batting diabetes, conducted at 12 leading medica
"has raised doubts as to their value in controlling
and its complications and, in fact, about their sa
institute said studies indicate that use of the drug
on "a greater risk of death from coronary heart c
than use of diet plus insulin or diet alone." It was
mended that the drugs be used only in patients w
maturity-onset diabetes in whom the disorder ca
controlled by diet alone or by diet plus insulin.

There are other forms of diabetes mellitus in a
the two major ones. Pregnant women sometimes
afflicted with gestational diabetes but return to n
after delivery. However, these women should co
watch their weight and have frequent checkups b
about 30 to 40 percent of them will develop diab
within 5 to 10 years. A condition formerly know
diabetes now is called impaired glucose tolerance
be treated by diet and weight loss, if necessary, t
actual diabetes from developing. When certain c
are induced by drugs, chemicals or diseases of th
or endocrine glands, secondary diabetes results.
on the severity, this form of the disease is treated
diet and insulin.

Since insulin must be injected under the skin,
should be taken in its administration. Most diab
including children, are capable of administering
tions themselves. The skin of the arm, abdomen
are considered the most convenient sites for inje
prevent thickening of tissue at the site of injectio
should be developed to avoid using the same inj
point. Authorities say the same puncture hole sh
used more than once every month or two.

Except for infants, the very young and the dis
betic patients must take full responsibility for th
care. All Type I and some Type II diabetics mus
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comparatively normal manner. The injections m

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given in precise doses at precise times and must be balanced with food consumption and physical activity. This requires measurements several times a day, either through a urine test that provides an indirect check on blood sugar levels or through a direct method of analyzing a single drop of blood in a home medical device. The single drop can be obtained by pricking the finger.

Some diabetics can get further help from a recently developed insulin pump. This device provides a predetermined, continuous dose of insulin throughout the 24 hours. Additional pre-meal doses of insulin can be given by pushing a button on the pump.

Sleep Sentry is a recently approved device that monitors insulin-dependent diabetics while they sleep and warns them of skin temperature drops and perspiration—two frequent symptoms of hypoglycemia. The device is worn on the wrist and is similar in appearance to a wristwatch.

Exercise is one way to avoid many of the complications associated with diabetes. If a diabetic is in otherwise good health, walking is recommended—provided warm-up routines are followed first. Prescribed sports activities also are recommended under the supervision of a physician or podiatrist.

Although diabetes is a complex disorder, its long-term complications chiefly affect blood vessels, nerves, kidneys and the eyes. Type I diabetics generally are more severely affected by complications.

Diabetic patients, particularly those with very high blood sugar, are more prone to infection because white blood cells that ordinarily fight infection do not work properly when sugar levels are too high. As a result, bacteria and other organisms may invade tissues rapidly and cause inflammation, abscesses and occasionally sepsis, a blood-borne infection. Women who have diabetes are more likely to give birth to babies with birth defects or who are stillborn; they are also somewhat more likely to die in childbirth.

Several years of poorly controlled diabetes can cause neuropathy, a complication arising when elevated blood sugars result in the deposit of glycoproteins (a sugar-protein complex) in the nerves. This is more likely to happen in the feet and legs. When it does occur in the feet there is a decrease in sensation because of the damaged nerves. A diabetic who is not watchful could be injuring his or her feet for days without being aware of it. For example, a patient who has difficulty telling the difference between hot and cold or sharp and dull could walk for days on a tack protruding through the shoe. A pebble lodged in the shoe could cause a similar injury that could lead to infection and gangrene. Similarly, many patients end up losing a leg because they fail to test bath water with a hand instead of a foot or because they sleep with hot water bottles, electric blankets or heating pads set too high and burn themselves.

Diabetics should inspect their feet regularly for cuts, redness, swelling or sores. They also should have regular foot examinations by a physician or podiatrist.

Diabetes, hypertension, excessive cholesterol and cigarette smoking are believed to be major contributors to premature hardening of the arteries. Diabetics in particular are subject to narrowing of the arteries in the lower extremities. The most common symptom of poor circulation is pain in the calves while walking. Other indications are diseased and irregular toe nails and feet that turn bright red when sitting with feet hanging down. Circulation may improve dramatically if a person conquers addiction to cigarettes. Medication and exercise also can help, as can a surgical bypass of the narrow arteries of the leg.

Neuropathy or poor circulation or occasionally both can cause a diabetic foot ulcer, an opening in the skin forming a small crater. If bacteria are growing in the ulcer it is known as an infected ulcer. Persistent infection may involve bones in the feet and turn to osteomyelitis. Gangrene, one of the most feared complications of diabetes, occurs when overwhelming infection is present in a localized area of the foot and death of that tissue results.

Type II diabetes may be treated conservatively with bed rest and antibiotics. In addition, podiatrists frequently can improve ulcers by using foot supports to redistribute weight when the patient walks. Neglect of osteomyelitis or gangrene can result in amputation.

Diabetics also must be especially concerned about their eyes. A few diabetics may develop long-term retinopathy, a condition caused by hemorrhages, fat deposits and scar formation behind the eye. Once again, part of the circulatory system is involved, this time the capillaries (tiny blood vessels). A patient should see an ophthalmologist as soon as diabetes is diagnosed and have a visual check at least once a year or more often if the physician recommends. This way, patients can be considered for treatment while the therapy can do some good.

Diabetes is a misfortune, but with personal care and discipline and medical supervision, a victim can lead a nearly normal life. Medical research continues into factors that trigger diabetes, the development of new drugs to control the disease, and even an inoculation against juvenile-onset diabetes. Meanwhile, those who have it can learn to live with it.

John M. Couric is a writer-editor with FDA's National Center for Drugs and Biologics.

RDAs: Key To Nutrition

by Chris Lecos

How can a consumer make sensible food choices to provide nutritious meals for the family when bombarded daily with messages, claims and advice about which foods to buy and confronted with the bewildering stock of foods on supermarket shelves?

It isn't always easy. A conscientious food shopper must do some planning to choose foods with the nutrients essential to good health.

For most Americans, the most readily available source of nutrient information is the nutrition label that appears on many, but not all, food products. The Food and Drug Administration created the nutrition label to make it easier for shoppers to compare food brands and their nutrient content. Although FDA is at present studying various ideas for revising and simplifying the nutrition label (see October 1982 issue of *FDA Consumer*), until something better is devised, it is still one of the most reliable aids available to consumers.

Ten years ago FDA first presented proposals for nutrition labeling of foods, an effort that one writer described as "one of the most ambitious programs" the agency had ever undertaken, in which government, the food industry, nutrition experts and consumers all played an active role.

More than 3,000 responded to FDA's proposals in 1972, and final regulations published the following year spelled out federal requirements for nutrition labeling. The result has been a larger number of foods with useful nutrition information, partly because it was mandatory for some food producers to include labels on their products and partly because industry voluntarily made the information available.

EXTRA
BARTLETT PEAR
BEST
SUGAR CORN

The recommended allowances, in effect, represent the amounts of essential nutrients that are considered adequate to meet the known nutritional needs of most healthy persons in the United States.

Under FDA's regulations, any food to which a nutrient is added or for which a nutrition claim is made must have a nutrition label. Recent FDA studies show that about 44 percent of packaged food sales in the United States involve products with nutrition labeling. About half of these bear the labeling because the producers are required to do so and about half because the manufacturers choose to include the information on their products.

The label includes two important areas of information for the consumer.
One discloses the number of
in a specified serving of a fo
with the amount—expressed
grams—of protein, carbohy
fat in a serving (there are ap
mately 28 grams in an ounce
other, under the heading "P
of Recommended Daily All
(U.S. RDA)," tells the consu
approximate amounts of cer
tial vitamins and minerals c
a serving. These amounts ar
expressed as percentages.

FDA established recomm
daily allowances for protein
vitamins and minerals in its
lations. However, under the
tions, percentages in a servi
required only for protein, fi
(vitamins A and C, thiamine
flavin and niacin) and two n
(calcium and iron). A manu
has the option of listing the
12 vitamins and minerals. T
are optional are vitamin D,
vitamin B_6, folic acid, vitam
phosphorus, iodine, magnes
copper, biotin and pantothe
any of the 19 are added to a
claim is made about them, t
would have to include all th
nutrition information.

As discussed later in this a
U.S. RDAs are based on rel
scientific information about
nutrient requirements. An e
of why certain vitamins and
should be consumed is not r
the consumer can accept the
the levels recommended are
deemed best for a healthy di

What the consumer needs
stand are the percentages an
use them. The shopper shou
that 25 percent of the RDA
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serving is good for one-four
person's recommended daily

The availability of this ki
information was an importa
for consumers. Until the U.S
were established by FDA, n
information on foods was q
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allowances replaced what w

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as the "Minimum Daily Requirements." The latter, adopted by FDA in 1940, were specified in earlier FDA regulations for declaring the nutrient values in foods for special dietary use and for dietary supplements of vitamins and minerals.

The MDR system, however, produced confusion and widespread dissatisfaction. FDA summarized the problem in the *Federal Register* in January 1972: "The continued existence of the term 'Minimum Daily Requirements' has led to the production, promotion and sale of a variety of dietary supplements that contain large multiples of the minimum daily requirements for vitamins and minerals, and by far exceed the adequate human total daily dietary requirements."

FDA's recommended daily allowances were derived mainly from the extensive nutrition data published by the Food and Nutrition Board of the National Academy of Sciences-National Research Council. Using the expertise of nutrition specialists and scientists, the National Academy issues what is known as recommended dietary allowances for a wide variety of age and sex groups in the general population. Its recommendations are based on an extensive review of current research and knowledge in the nutrition field.

The publication of recommended dietary allowances by the National Academy began in 1943, primarily as a World War II planning guide for the general population and military services. Its early recommendations focused on calories and nine nutrients. The number of nutrients for which standards were proposed grew and the standards were revised, where necessary, as scientists learned more about human nutritional needs.

As indicated, the National Academy's recommendations are for general population groups, as are FDA's recommended daily allowances. The recommended allowances, in effect, represent the amounts of essential nutrients that are considered adequate to meet the known nutritional needs of most healthy persons in the United States. They do not, however, take into account the special needs of people required to follow special diets because they are ill or suffering from other medical disorders that require professionally supervised diets. Those are special problems beyond the scope of the dietary recommendations made.

EXTRA
BARTLETT PEARS
BEST
SUGAR CORN

The availability of this kind of information was an important advance for consumers.

There is a further qualification. While they are presented as daily allowances, this does not necessarily mean the intake levels recommended need to be met religiously each day. Because the body is able to store some nutrients for later use and can endure lower-than-required intakes for short periods without harm, the recommended dietary allowances can be met from diets that fulfill the nutrient requirements over a five- to eight-day period.

When FDA adopted its nutrition labeling regulations in 1973, it based its recommended daily allowances (or U.S. RDAs) in part on the nutrient values published by the National Academy in 1968. Although some changes have occurred in the academy's dietary allowances since then (the most recent were made public in 1980) the modifications were considered so minor that they did not warrant any changes in the U.S. RDAs.

FDA's recommended daily allowances apply to four general population groups (compared to 26 groups listed in the National Academy's 1968 report). This was done to make it simpler and easier for consumers to use the information on a label. The four population groups for which U.S. RDAs were established were for infants up to 1 year; for children (junior foods) under 4 years; for persons who are 4 years and older (most food products are based on these allowances); and for pregnant or lactating women.

The amounts of protein, vitamins and minerals shown as percentages on a food label simplify the consumer's task of comparing foods for their nutrient quality. Instead of having to refer to complex and technical tables, as published by the National Academy, to determine if they are obtaining enough of given nutrients, consumers can simply add the percentages for each nutrient. FDA's allowances are based generally on the highest values recommended in the National Academy's findings. For that reason, many normal, healthy people would not necessarily have to consume 100 percent of the U.S. RDA of a given nutrient each day.

Chris Lecos is a member of FDA's public affairs staff.

The Notebook

The Notebook: a potpourri of items of interest gathered from FDA news releases, other news sources and the Federal Register *(designated* FR, *with date of publication). The* Federal Register *is available in many large public libraries.*

- **non-prescription antacids**: Labels on **non-prescription antacids** can now include the term "upset stomach" to describe symptoms associated with heartburn, sour stomach or acid indigestion. The effective date of the new FDA ruling was Sept. 30 (*FR* Aug. 31).

■ FDA is seeking information on the abuse potential, actual abuse and trafficking of four **sedative-hypnotic drugs** (chlorohydrate, paraldehyde, phenobarbital and potassium bromide) and five **analgesics** (buphrenorphine, butorphanol, cyclazocine, nalbuphine and pentazocine). The information will be submitted to the World Health Organization, which is considering whether to recommend international restrictions on these drugs (*FR* Aug. 31).

■ July 1, 1985, is the new uniform effective date by which food manufacturers must comply with **food labeling regulations** adopted by FDA after Aug. 13, 1982, and before July 1, 1984. Use of a uniform effective date provides for an orderly and economical industry adjustment to new labeling requirements by allowing sufficient lead time to develop new labeling materials (*FR* Aug. 13). Among the major proposals that could come under that 1985 date is the sodium labeling measure that would include sodium content listing on nutrition labels.

■ The standard of identity for **canned peas** may be amended to reinstate magnesium hydroxide, magnesium oxide and magnesium carbonate as optional ingredients. FDA deleted them from the standard, effective April 1981, because it was thought they were no longer used in the United States. A recent petition indicates a canner of peas is interested in using magnesium compounds in canned peas (*FR* Aug. 31).

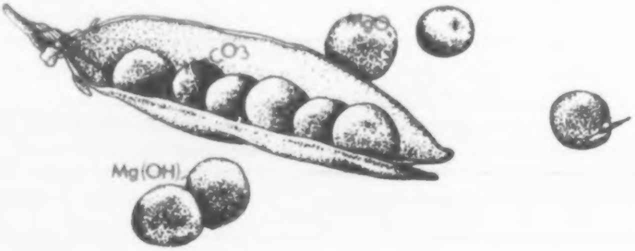
■ The U.S. Department of Agriculture has issued a final rule permitting the use of fresh, frozen or cured beef or veal or combinations, or pork or combinations with beef or veal, in **braunschweiger and liver sausage**, and beef fat in braunschweiger (*FR* Aug. 19).

■ Standards of identity for **cranberry juice cocktail, artificially sweetened cranberry juice cocktail, lemonad and colored lemonade**, originally established in April and May of 1968 and put on hold in July of 1968, have been revoked. This means that these products are nonstandardized foods and are subject to FDA's ingredien labeling requirements (*FR* Aug. 6).

■ The Environmental Protection Agency has issued a final rule amending portions of its regulations on use o **PCBs in electrical equipment**. The amendments, which became effective on Sept. 24, prohibit use and storage for reuse of PCB transformers or electromagnets that pose an exposure risk to food or feed. The effective dat is Oct. 1, 1985. PCB transformers are to be visually inspected once every three months (*FR* Aug. 25).

■ FDA is proposing to amend its biologics regulation to reduce the number of samples of **hepatitis diagnostic test kits** manufacturers must submit for testing prior to marketing. The proposed rule will eliminate unnecessar burdens on both manufacturers and the agency (*FR* Aug. 17).

■ **RIMSO-100**, a DMSO product manufactured by Research Industries Corp., Salt Lake City, Utah, is not available over the counter for reagent and drug use, no matter what was said in the February 1982 edition of th *DMSO Report*, an Oregon newsletter. FDA says the product does have a legitimate use as a cryopreservativ (freezing solution) for certain blood components, but distribution for drug use would violate new drug provisions of the Food, Drug, and Cosmetic Act. The agenc has advised the manufacturer of its responsibility to sel RIMSO-100 only to firms known to have the capabilit to freeze blood components, such as blood centers and large hospital blood banks.



Investigators' Reports

Dalton's Deception

A clinical investigator tests new drugs. He is required to monitor the health of the patients and keep accurate records. If all goes well, and the drug is proven safe and effective based on these trials, the product can then be sold. But all didn't go well in the case of Dr. Fred C. Dalton, a psychiatrist and clinical investigator in Mineola, N.Y. On May 11, 1982, he was charged with two counts of falsifying data, convicted, fined $1,000 and disqualified from participating in future new drug studies.

Dalton's troubles stemmed from his clinical research on the drug Dothiepin, a tranquilizer used for treating depression. Marion Laboratories Inc., Kansas City, Mo., sponsored the new drug and hired Dalton from 1972 to 1975 to conduct the patient tests. The written protocol (a plan setting forth how clinical trials will be conducted) required all 30 patients to have electrocardiograms (EKGs), ophthalmological exams and blood and urine tests, as well as personality tests.

When representatives from Marion visited Dalton's office in July 1977 to review patient records and compare his results with those of other clinical investigators participating in the study, Marion noticed that Dalton's results were oddly uniform. Patients receiving Dothiepin showed immediate and sharp improvement; patients given a comparison drug showed much less improvement; and patients in the placebo group showed no improvement.

Three months later Marion Laboratories tried talking to Dalton to find out if he had broken the patient code, a means of concealing from the investigator which patient receives the placebo and which the real product. Dalton said that he didn't know the code and that his results were accurate. Dissatisfied, Marion Laboratories ended Dalton's participation in the study and in November 1977 submitted Dalton's records to FDA, as required by law.

FDA reviewed Dalton's records and those of two other physicians and one laboratory, the Center for Laboratory Medicine in Mineola, all of whom had done tests for the psychiatrist. The discrepancies were apparent.

Forty-eight of the 51 eye examination reports submitted by Dalton contained false information; dates and signatures were also suspect. Only 3 of the 52 EKGs submitted by Dalton to Marion Laboratories corresponded completely with the records kept by the physician who performed the tests. In about 20 cases, results from the EKGs were completely false.

Blood and urine tests were no different. Dalton produced such records for 26 of the patients in the study, yet the Center for Laboratory Medicine, where the tests were conducted, had records for only 16 individuals.

FDA filed charges in the U.S. District Court for the Eastern District of New York, in Brooklyn, N.Y., and Dalton pleaded guilty to creating false, fictitious and fraudulent records of ophthalmologic tests and laboratory test results.

FDA Seizure Upheld

April 1980 was more than just income tax time for Goshen Labs, Goshen, N.Y. U.S. marshals seized $71,000 worth of finished animal drugs and raw materials from the veterinary drug firm for two types of violations. The company protested the seizure, claiming their products were "grandfathered" and thus were exempt from FDA's new animal drug regulations. FDA took a different view. Two years later the U.S. District Court for the Southern District of New York upheld the agency's charge that Goshen was selling unapproved new animal drugs.

Goshen's problems involved more than unapproved drugs. For several years the firm had failed to comply with FDA's Good Manufacturing Practices, including quality control, sanitation, packaging and labeling requirements. In October 1979 FDA sent Goshen a regulatory letter outlining the violations of the GMPs and new animal drug regulations. Agency representatives even sat down with the company management and explained the regulations and how to comply with them.

Reinspection of the firm by the **Buffalo district** office showed no improvement, and in April 1980 U.S. marshals seized all finished products manufactured by the firm, including several new animal drugs distributed by the firm without New Animal Drug Applications and 200 kinds of raw materials (totaling 3,100 pounds and packaged in more than 230 various containers). Some of the containers appeared very old and bore illegible labeling. Some contained toxic substances such as arsenic trioxide and xylene.

Goshen Labs not only claimed its products were "grandfathered" but rebutted the charge of GMP violations by arguing it had never had a problem with any of its drugs.

Cracked Necks

No imperfection is too slight to overlook when it comes to ensuring drug purity. Last June, a total of 711,184 vials of an anti-infection drug were destroyed because of hairline cracks in the necks of some of the vials.

The drug, lyophilized flagyl I.V., sold by Searle Pharmaceuticals Inc., Skokie, Ill., is prescribed for trichomonas infections. Originally in a liquid state, the drug is dried and packaged in vials. When ready to be used, it is reconstituted with sterile water and injected intravenously into the patient.

Problems with the product were reported to Searle between December 1980 and May 1981. Some reports said the vials exploded after water was added for dilution. Others said the powder could be seen outside the rim of the seal. FDA's **Chicago district** office learned of the problems through drug product defect reports.

The drug was made for Searle by Elkins-Sinn Inc. of Cherry Hill, N.J. It is believed that the cracked necks resulted from excessive pressure placed on the seals during the assembly process.

Elkins-Sinn Inc. has since increased its inspections and improved its quality control procedures. Searle initiated a Class II recall of all lots of flagyl I.V. by sending letters and Mailgrams to hospital pharmacists and administrators nationwide.

The condemned vials were returned to Searle's warehouse in Elk Grove Village, Ill., where they were crushed by four compactor garbage trucks, hauled to a landfill in Glenview, Ill., and buried on June 8, 1982.

A Tale of Two Warehouses

Two Seattle Oriental food warehouses, beset by insect and rodent infestation, have solved their problems and are back in the business of providing clean and orderly food storage.

Mekong Market, the first, held many kinds of rice products. When **Seattle district** office inspectors visited the firm in April 1982 they found mice on the floor, rodent-defiled food products and Indian meal moths in one lot of rice. The mouse and insect infestation was serious enough for FDA to initiate a seizure in May 1982.

The firm reconditioned the rodent-contaminated food, destroying about 6,000 pounds at a landfill in Seattle. The firm also segregated the insect-infested lot of rice, pending a decision as to its disposition. However, when FDA investigators returned to the firm they found that the insect infestation had spread to 60,000 pounds of rice which had already been reconditioned. The firm then fumigated the rice and shipped it to a California

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The second Seattle war
similar problems. The Yic
housed dried fish, salted p
and noodles, among other
foods. Scattered among th
cases of food products we
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U.S. marshals seized all
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Mora Trouble?

Although it was called a
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unit offered for import fro
looked more like an acupu
device to inspectors at FD
Louis station in Missouri.
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FDA had determined that it could be legally imported.

FDA found that it could not. The Bureau of Medical Devices at FDA headquarters told the St. Louis station that the unit was a Class III medical device, meaning that the manufacturer was required to show that it was safe and effective for its intended uses. This had not been done. Also, the unit had been made by a foreign manufacturer not registered with FDA, and the unit did not include adequate instructions for safe use.

Because of these several violations, the unit (with a declared value of $4,862) was refused entry and was returned by Customs officials to the manufacturer.

Grain Is Salvaged

Grain elevator explosions are not uncommon in the Plains States and upper midwest sections of the United States. Fine dust from the stored grain floats through the huge concrete structures and, despite strict safety precautions, can be ignited by a chance spark or even an electric switch. Then the towers explode and collapse on themselves, reduced to piles of rubble. When this happens, FDA investigators must check through the damaged grain to see what can be salvaged.

A dust explosion earlier this year destroyed a 200-foot elevator in Council Bluffs, Iowa, killing five workers and injuring many others. When firemen arrived, they discovered that fire hydrants had been broken or were buried under tons of concrete and grain and that no water was available to fight the fire. Two railroad tank cars were quickly filled with water a few blocks away, and a Union Pacific railroad engine pushed them onto a siding near the elevator site. The firemen used that water to bring the fire under control.

When an FDA investigator from the **Kansas City district** arrived to oversee the grain salvage work, he learned that one tank car had contained sludge, a byproduct of railcar cleaning. The grain to be salvaged may have been wetted down with water from that car.

The investigator sent a sample of the water still in the car and several samples of the grain to the FDA laboratory in Kansas City. The laboratory found polychlorinated biphenyls in the water sample, but no detectable PCBs in the grain. With that assurance, the investigator allowed the salvage operation to continue. When salvage was completed, more than 1.5 million bushels of corn and soybeans had been reconditioned and converted into animal feed.

Correction:
On Report of Oyster Seizure

A shipment of oysters seized by FDA in Baltimore did not come from "contaminated Virginia waters" as stated in the May 1982 Investigators' Reports. They were uncertified and subject to seizure because they were shipped by an unlicensed Virginia packer. Cloyde W. Wiley, director of the Bureau of Shellfish Sanitation, Virginia Department of Health, supplied this clarification.

—This small sample of reports from the field was compiled and written by Marti Asner, Louise Fenner and Richard Thompson.

Seizures and Postal Service Cases

FILED SEIZURE ACTIONS charge violations of the Federal Food, Drug, and Cosmetic Act and are initiated based upon FDA recommendations. A seizure action is commenced by the filing in the U.S. district court where the goods are located. A U.S. marshal is then directed by the court to take possession of the goods, removing the product from commerce, until the matter is resolved.

A total of 7 actions to remove from the consumer market products charged to be violative was reported in August. These actions included 3 seizures of foods with charges concerning contamination and insanitary handling. Others included 4 of drugs.

PRODUCT, DISTRICT & DATE FILED	FIRM & PLACE OF BUSINESS	CHARGES
FOOD/Contamination, Spoilage, Insanitary Handling		
Flour, beans, whole wheat meal, and other food stocks/U.S. District Court for the Southern District of West Virginia 7/14/82	Crook Product Co./Beckley, W. Va.	Certain of the foods contain rodent and bird filth, and all of the foods have been held under insanitary conditions.
Fruit cocktail, canned/U.S. District Court for the Eastern District of Arkansas 6/29/82	Shipped from Tipton, Ind.	Product was held in swollen cans.
Peanuts/U.S. District Court for the Eastern District of Virginia 7/22/82	Hancock Peanut Co. Inc./Courtland, Va.	Products have been held under insanitary conditions.
DRUGS/Human Use		
A-Van pentylenetetrazol capsules/U.S. District Court for the Western District of Tennessee 8/12/82	D. M. Graham Laboratories Inc./Hobart, N.Y.	Product is a new drug without an effective approved New Drug Application.
Cough syrups/U.S. District Court for the District of New Jersey 7/13/82	Anything & Everything/Brooklyn, N.Y.	Products are new drugs without effective approved New Drug Applications and are misbranded in that the products' labeling falsely and misleadingly represents and suggests that the drugs contain specific amounts of chloroform, which representation and suggestion are contrary to fact because chloroform is not present in the labeled amounts.
Myco Triacet Cream/U.S. District Court for the Western District of New York 6/17/82	Lemmon Co./South Hackensack, N.J.	Circumstances of the product's manufacture, processing, packing and holding failed to conform with current Good Manufacturing Practice.
Nicozol pentylenetetrazol capsules and pentylenetetrazol elixir/U.S. District Court for the Western District of Tennessee 8/12/82	Vale Chemical Co. Inc./Allentown, Pa. Pharmaceutical Associates Inc./Greenville, S.C.	Products are new drugs without effective approved New Drug Applications.

U.S. POSTAL SERVICE

actions taken in medical cases as authorized in the Mail Fraud Statute (18 U.S.C. 1341) and/or the False Representation Statute (39 U.S.C. 3005) as reported by the Chief Postal Inspector.

Complaints Filed by Law Department Under 39 U.S.C. (False Representation)

May 21, 1982: **Body Science**, 20 Medford Ave., Patchogue, N.Y. Advertising and sale through the mail of the product "SEA-10," representing the ability to "help thicken the cynovial fluid that lubricates the joints so it doesn't become watery and leak through tiny holes in the membrane."

June 4, 1982: **Bee Pollen From England**, P.O. Box 636, Newton Lower Falls, Mass. Advertising and sale through the mail of the product "Bee Pollen From England." The ad states, in part, "the energy pill is here. A patented natural food supplement can be the answer for housewives, dieters, joggers, business people—anyone who wants more energy. Athletes training on English bee pollen daily recover energy faster after exercise and fatigue. It's amazing how this natural product improves recovery power."

False Representation Orders Issued by Judicial Officer Under 39 U.S.C. 3005

March 19, 1982: Against **Bob's Sundries Inc.**, P.O. Box 7908, Pittsburgh, Pa. Satisfactory evidence was presented to the Postal Service that Bob's Sundries Inc. and its representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising "Stimulants." These stimulants are being sold as look-alike narcotics.

April 5, 1982: Against **Speciality Sales Co.**, 130 Buenta Vista Ave., Yonkers, N.Y. Satisfactory evidence was presented to the Postal Service that Speciality Sales Co. and its agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Sauna-Slimmer." The ad states, in part, "reduce waist and stomach bulges in 3 days . . . lose unwanted inches, tighten sagging muscles—without diets or exercise. Now you can quickly trim embarassing bulges the safe effortless way."

April 23, 1982: Against **Formula Four Inc.**, P.O. Box 81262, Chamblee, Ga. Satisfactory evidence was presented to the Postal Service that Formula Four Inc. and its representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Jennifer Lord Formula #714." The ad states, in part, "is the first natural, nonsurgical way to enlarge your breasts that makes sense. It utilizes the body's own breast development mechanism to improve your natural appearance and self-confidence . . . best of all, it works!"

April 23, 1982: Against **Formula Four Inc.**, P.O. Box 81262, Chamblee, Ga. Satisfactory evidence was presented to the Postal Service that Formula Four Inc. and its agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Total Control." The ad states, in part, "cellulite! You can do more than be self conscious about it. Total Control starts getting rid of cellulite immediately."

May 27, 1982: Against **Leucadia Pharmacals**, 103 N. Highway 101, Leucadia, Calif. Satisfactory evidence was presented to the Postal Service that Leucadia Pharmacals and its representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Prost-Rite Tablets." The ad states, in part, "relief of the most common prostate trouble—benign prostatic hypertrophy . . . all natural ingredients—proven effective in 2 separate clinical tests published in leading medical journals."

June 11, 1982: Against **Slim Suit**, 175 Fifth Ave., New York, N.Y. Satisfactory evidence was presented to the Postal Service that Slim Suit and its agents are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Slim Suit," representing the ability to "lose weight while you sleep! Slimsuit, the sensational body trimmer, no exercise, no dieting, no drugs . . . quickly melts away excess weight and fluid without any effort on your part."

June 21, 1982: Against **Athena Products Ltd.**, P.O. Box 81112, Chamblee, Ga. Satisfactory evidence was presented to the Postal Service that Athena Products Ltd. and its representatives are engaged in conducting a scheme or device to obtain money by means of false representation. The firm was advertising the product "Pollen-Ade - Bees Pollen." The ad states, in part, "pollen-ade gives you the energy and vitality to go further than you've ever gone before. The bee pollen used in pollen-ade has been shown to greatly increase vitality and physical endurance by stimulating the production of more energy. Pollen-Ade can also improve circulation and even alleviate many allergic symptoms including hay fever."

Notices of Judgment

NOTICES OF JUDGMENT on Seizure Actions

FOOD/Contamination, Spoilage, Insanitary Handling

Aniseed, rosemary leaves, chanadal beans, and **marjoram leaves,** at Brooklyn, E. Dist. N.Y.

Charged 8-21-80: while held by Purity Millers Inc., Brooklyn, N.Y., one lot of aniseed and one lot of marjoram leaves contained rodent and/or insect filth, and all of the articles had been held under insanitary conditions; 402(a)(3), 402(a)(4).

The various owners of the articles claimed the articles and subsequently authorized the dealer to file and maintain their respective claims on their behalf. Ultimately, a consent decree authorized release of the articles to the dealer for salvaging. (F.D.C. No. 63133; S. No. 80-194-017 et al.; N.J. No. 1)

Black-eyed peas, dried, at Wasco, E. Dist. Calif.

Charged 9-29-81: when returned to Berger & Co./San Joaquin Crops Co. Inc., Wasco, Calif., the article contained rodent and insect filth and had been held under insanitary conditions; 402(a)(3), 402(a)(4). Consent decree authorized release to Berger & Co. for salvaging. (F.D.C. No. 63549; S. No. 81-265-787; N.J. No. 2)

Cheese, low-moisture, part-skim mozzarella, frozen, at Portsmouth, E. Dist. Va.

Charged 8-28-79: while held for sale, the article was unfit for food due to the presence of plastic-like particles and metal fragments; 402(a)(3).

The Massachusetts counsel for Cheese Corp. of America Inc., of Lawrence, Mass., and Amsterdam, N.Y., discussed the filing of a claim and answer in this action, but no person intervened in this action as required by the rules of the court. The purported owner of the article (Cheese Corp. of America Inc.) had submitted the requisite papers to the clerk of the court but had failed to obtain local counsel. On numerous occasions, the government advised of the need to obtain local counsel.

The clerk of Cheese Corp. of America Inc. advised that the corporation would appeal the denial of the corporation's right to appear and defend itself "per se," since the necessary papers were on file with the court and there was no reason why the action could not be transferred as was done with companion cases in other jurisdictions. Ten months after the action had been filed, a default decree of condemnation ordered the article destroyed.

The article was destroyed pursuant to the default decree. The purported owner of the cheese filed a notice of appeal, but the court refused to accept an appeal because the corporation had never become a party to the proceeding. (F.D.C. No. 62406; S. No. 79-151-598; N.J. No. 3)

Garbanzo beans, white beans, farina, chocolate-flavored drink mix, and **cornmeal,** at Mayaguez, Dist. Puerto Rico.

Charged 12-3-81: while held by Sucesores de Esmous & Co. Inc., Mayaguez, Puerto Rico, the articles had been held under insanitary conditions; 402(a)(4). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63590; S. No. 81-281-761; N.J. No. 4)

Peppers, jalapeno, pickled, canned, at El Paso, W. Dist. Texas.

Charged 4-12-82: while held for sale, the article was held in swollen cans; 402(a)(3). Default decree ordered destruction. (F.D.C. No. 63697; S. No. 82-266-692; N.J. No 5)

Pinto beans, dried, at Portales, Dist. N.M.

Charged 3-1-82: while held by Portales Valley Mills Inc., Portales, N.M., the article contained rodent urine and had been held under insanitary conditions; 402(a)(3), 402(a)(4). Default decree ordered destruction. (F.D.C. No. 63640; S. No. 82-266-854; N.J. No. 6)

Rice, at Mineola, E. Dist. Texas.

Charged 5-20-81: when shipped by Western Rice Mills Inc., McGehee, Ark., the article contained insect filth and had been prepared, packed and held under insanitary conditions; 402(a)(3), 402(a)(4). Consent decree authorized release to the shipper for salvaging. (F.D.C. No. 63273; S. Nos. 81-210-591/2; N.J. No. 7)

Rice, candy, and **dried codfish,** at Bronx, S. Dist. N.Y.

Charged 2-19-82: while held by 37 & 38 Bronx Terminal Produce Inc. (Las Villas), and 37 & 38 Bronx Terminal Market, Bronx, N.Y., one lot of rice and the lot of dried codfish contained rodent filth, and all of the articles had been held under insanitary conditions; 402(a)(3), 402(a)(4). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63639; S. No. 82-138-324 et al.; N.J. No. 8)

FOOD/Economic and Labeling Violations

"Flounder" fillet-portions, at Windsor Locks, Dist. Conn.

Charged 12-12-79: when shipped from Watertown, Mass., the article, labeled in part "High Liner North Atlantic Flounder . . . Flounder Coated with 'Flavor-Tex' . . . National Sea Products (U.S.) Corp., Tampa, Florida," had had Greenland turbot substituted for flounder—402(b)(2); the article's labeling was false and misleading in claiming that the only fish in the article was flounder—403(a)(1); Greenland turbot was offered for sale under the name of another food—403(b); and the article's label lacked the common or usual name for Greenland turbot and of each ingredient, because "flounder" was not the common or usual name for Greenland turbot—403(i)(1), 403(i)(2). Before allowing the entry of a default decree, the court ordered FDA to enter the custodian's warehouse for inspecting and testing of the article to determine its fitness for human consumption and for the appropriateness (due to time in storage, the article might no longer be fit for human consumption) of delivering the article for charitable distribution. Due to the delay, the article was destroyed by the custodian. (F.D.C. No. 62695; S. No. 80-160-603; N.J. No. 9)

"Honey," at Ponchatoula, E. Dist. La.

Charged 12-10-81: when shipped by Anthony Syrup Co. (Oliver Anthony), Philadelphia, Miss., the article, labeled in part (38-oz. and 20-oz. jars) "Anthone's Wild Flower Brand Honey Packed by Anthony Syrup Co. . . . Philadelphia, Miss. . . . [and 20-oz. jars only: 'Ingredients: Honey, corn sweetner [sic] and citric acid']," had had glucose syrup (in the 38-oz. jars) and corn syrup (in the 20-oz. jars) substituted wholly or in part for honey—402(b)(2); the article's labeling was false and misleading in claiming the article to be honey—402(a)(1); and the article was also in violation of the Fair Packaging and Labeling Act, since the net quantity of contents statements were not expressed in fluid ounces followed in parentheses by a declaration of the largest whole unit—15 U.S.C. 1453(a)(3)(A)(i). Default decree ordered destruction. (F.D.C. No. 63599; S. Nos. 82-281-395/6; N.J. No. 10)

FOOD ADDITIVE

Beverage mixes, Sun-Ripe Diet Lem and Sun-Ripe Lem-Or, at Cedar Grove, Dist. N.J.

Charged 4-29-81: while held by Concentrates Co. Inc., Cedar Grove, N.J., after manufacture locally from interstate sugar, the articles contained the non-conforming food additive saccharin, since the articles (which contained sugar and which were intended for use as mixes for alcoholic beverages) were not for a valid special dietary use; 402(a)(2)(C). The articles were claimed by the dealer. The claimant agreed to reformulate and relabel its food products purporting to be diet or reduced calorie mixers and to consent to a decree of destruction, without any admission concerning the issue of violations. (F.D.C. No. 62318; S. No. 81-274-386; N.J. No. 11)

DRUGS/Human Use

Allopurinol tablets, and **other specified drugs**, at Hollywood, S. Dist. Fla.

Charged 2-12-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). The shipper intervened, denied the charge, claimed the articles, and demanded a jury trial. Thereafter, pursuant to stipulation of the parties, the action was consolidated for trial with a similar action in the District of New Jersey. Ultimately, a consent decree ordered the articles destroyed. (F.D.C. No. 62771; S. No. 80-193-371 et al.; N.J. No. 12)

Diethylpropion HCl tablets, at Valley Stream, E. Dist. N.Y.

Charged 12-12-78: when shipped by Pharmadyne Laboratories Inc., Hackensack, N.J., the article was a new drug without an effective approved New Drug Application; 505(a). The shipper intervened and claimed the article. The action was consolidated for trial in the District of New Jersey, with similar actions. Ultimately, a consent decree of condemnation ordered the article destroyed. (F.D.C. No. 61980; S. No. 79-139-805; N.J. No. 13)

Furosemide tablets, furosemide, and **in-process furosemide powder**, at Hackensack, Dist. N.J.; **furosemide tablets** (a lot returned from Hialeah, Fla.), at Hackensack, Dist. N.J.; **triamterene with hydrochlorothiazide capsules**, at Elmwood Park, Dist. N.J.; and **triamterene with hydrochlorothiazide capsules**, and **other specified drugs**, at Elmwood Park., Dist. N.J.; four seizure actions.

Charged on or about 3-28-79, 1-22-80, 3-18-80, and 3-13-80: while held by Pharmadyne Laboratories Inc., of Hackensack, N.J. (and subsequently of Elmwood Park, N.J.), which was using interstate furosemide, triamterene with hydrochlorothiazide, and other interstate components in manufacturing finished drugs, the articles were new drugs without effective approved New Drug Applications—505(a); and (all actions except the returned lot of furosemide tablets) the articles' labeling lacked adequate directions for use, and the articles were not exempted due to their New Drug Status—502(f)(1).

The articles were claimed by the dealer, who denied the charges, who asserted, as affirmative defenses, that the articles were not "new drugs" because they were generally recognized as safe and effective among qualified experts, and that the government was estopped because of the claimant's reliance upon the Lannett case (585 F.2d 575). The government served written interrogatories on the claimant. The government moved that this action be consolidated for purposes of discovery and trial. The actions were consolidated. Ultimately, a consent decree ordered the articles destroyed. (F.D.C. Nos. 62369, 62809, 62907 and 62911; S. Nos. 79-193-425, 80-208-590, 80-208-597, et al.; N.J. No. 14)

K. H. 3 procaine HCl & hematoporphyrine capsules, at Laredo, S. Dist. Texas.

Charged 5-5-80: when imported from England by Premier Inc., Laredo, Texas, the article, labeled in part "K.H. 3 Geriatricum Schwarzhaupt Oral Procaine Geriatric . . . Manufactured by Schwarzhaupt Ltd., Cork, Republic of Ireland," was a new drug without a New Drug Application; 505(a).

The article was claimed by Premier Inc., Laredo, Texas, who denied the charge and who moved to dismiss the action on the grounds that the court lacked jurisdiction, since the article was never in interstate commerce but was brought into the United States "in bond" and placed in an import and export warehouse.

The court denied the claimant's motion to dismiss, saying:

"Pending for consideration is a Motion to Dismiss filed by Premier, Inc. ('Premier'), the party in interest. The motion seeks dismissal on the grounds that the complaint fails to state a claim upon which relief can be granted. Rule 12(b)(6), *Fed. R. Civ. P.* The filing of such a motion has the legal effect of admitting all facts alleged in the complaint, and in deciding such a motion the Court must view the allegations of the complaint in the light most favorable to the Plaintiff. *Ward* v. *Hudnell*, 366 F.2d 247 (5th Cir. 1966). A motion to dismiss for failure to state a claim should not be granted unless it appears to a certainty that the plaintiff would not be entitled to recover under any state of facts which could be proved. *Cook & Nichol, Inc.* v. *Plimsoll Club*, 451 F.2d 505 (5th Cir. 1971).

"The fundamental deficiency in the motion to dismiss is reflected in paragraph 2 therein, where it is alleged that 'it appears on the face of the complaint . . . that said goods and items are not and never were in interstate commerce within the United States, but were brought into the United States "in bond" . . .' Nothing of the sort appears on the face of the complaint. Instead, the complaint simply alleges that the articles in question are presently in Laredo, Texas, having been imported into the United States via steamship from England. It is true that Premier's unverified answer alleges that the items were never in interstate commerce because they were brought into the United States 'in bond.' The court also realizes from reading Plaintiff's opposition to the motion that this unverified allegation by Premier may well be true. Nevertheless, the state of the record is such that a motion to dismiss could not be granted. Even if the Court were inclined to go outside the pleadings at this time, Rule 12(b)(6) would require that the pending motion be converted into one for summary judgment and disposed of accordingly. *See Underwood* v. *Hunter*, 604 F.2d 367 (5th Cir. 1979).

"The Court declines to convert the present motion into a motion for summary judgment. Even if proper documentation would be presented to establish that the items in question were actually shipped 'in bond,' other issues would remain for determination. Plaintiff has furnished the Court a copy of Findings of Fact and Conclusions of Law entered in *Laboratorios Kem, S. A.* v. *Fink*, Civil Action No.

76-804-N (S.D. Cal.). While that opinion is clearly in point, nevertheless the court there considered many factors which do not seem clearly established at this time in the present record. For example, the California court apparently had evidence that the Food and Drug Administration compiled an administrative record in a rule-making proceeding designed to determine whether the item in question was a 'new drug' and whether or not it was exempt under either of the so-called 'grand father issues' of 1938 and 1962. There was also evidence as to whether the item in question was intended for use in the treatment of man and whether any new drug applications or requests for exemptions were on file. No similar record is before the Court in the present case. There is an affidavit from Jerome A. Halperin expressing certain 'opinions' of the FDA as to the item in question but the Court is not satisfied at this point that such an affidavit would have the same import as a formal decision by the Commissioner of the FDA. Premier had indicated as early as June 24, 1978, that it was in the process of furnishing to the Court a brief on the issues presented, but no such brief has been discovered.

"For all of the foregoing reasons, Premier's Motion to Dismiss is hereby Denied. The Court hereby directs the attorneys for both parties to meet and confer forthwith toward the end of deciding how this case can be expeditiously concluded. The Court is prepared to give a trial setting as soon as the parties are ready. It may be possible for the parties to stipulate most if not all of the facts in the case, which would also expedite a final ruling, and they are encouraged to explore this possibility. The parties are further directed to correspond with the Court, and by copy to each other, no later than Dec. 5, 1980, advising the Court of the status of this case at that time, including whether or not the case is ready for trial and whether the parties feel that a formal pre-trial conference with the Court would be helpful."

The action was consolidated with three other seizure actions involving the identical law question based on virtually identical facts. The parties filed motions for summary judgment and agreed that the disposition of the motion for summary judgment would effectively terminate the actions. In ruling in favor of the government, the court said:

"The United States seeks condemnation of the boxes of K.H.3 on the grounds that they were brought into the United States in violation of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §301, *et seq.* (hereinafter 'the Act'). All facts necessary to disposition of this case have been stipulated to by the parties or are conclusively established by uncontested affidavits.

"Section 505(a) of the Act provides that 'No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) of this section is effective with respect to such drug.' 21 U.S.C. §355(a). . . . The Act provides that any new drug introduced into interstate commerce in violation of section 505(a) 'shall be liable to be proceeded against while in interstate commerce, or at any time thereafter, on libel of information and condemned . . . ' 21 U.S.C. §334(a)(1). Any new drug so condemned 'shall be disposed of by destruction.' *Id.* (d)(1).

"The parties have stipulated that the drug under seizure, K.H.3, is a 'new drug' within the meaning of 21 U.S.C. §321(p)(1), and that it is labeled for use in the treatment of disease in man. Further, that there is neither an approved 'New Drug Application' nor an 'Investigational Drug Exemption' in effect for K.H.3 and therefore the drug cannot come within the exemption of 21 U.S.C. §355. The only issues to be decided, then, are (1)whether the K.H.3 under seizure was introduced 'into interstate commerce' within the meaning of 21 U.S.C. §321(p); and (2)if so, whether the United States is equitably estopped from destroying the seized drugs because of the Government's alleged prior conduct in approving the entry of the drug into the United States for export as in-bond merchandise.

"The Court concludes that the K.H.3 under seizure was unquestionably 'introduced into interstate commerce,' and therefore is liable to be proceeded against by the United States. It is fundamental that Congress has the constitutional power 'to regulate Commerce with Foreign Nations, and among the several States. . . .' *U.S. Const. Art.* I §8, Cl.3. Such power is not confined to commercial or business transactions. Indeed, '[f]rom an early date such commerce has been held to include the transportation of persons and property no less than the purchase, sale, and exchange of commodities, *United States* v. *Hill*, 248 U.S. 420, 423, and goods may move in commerce though they never enter the field of commercial competition. . . .'

"Claimants urge, however, that the drugs were never introduced into interstate commerce because the drugs were transported 'in bond' from the United Kingdom and the Republic of Germany to the state of Texas, solely for the purpose of being exported to foreign countries. *See* Tariff Act of 1930, 19 U.S.C. §1553. While this argument undoubtedly has a certain surface appeal, it ultimately fails. Congress has explicitly precluded the bonding of 'merchandise the importation of which is prohibited.' K.H.3 cannot qualify for protection under the bonding statute since it clearly cannot legally be imported under 21 U.S.C. §355(a). *United States* v. *300 Oz. Gerovital Lotion*, 492 F. Supp. 114 (C.D. Cal. 1980); *Laboratories Kem, S.A., Inc.*, Civil No. 76-804-N (S.D. Cal. 1979). Therefore, as improperly bonded merchandise introduced into interstate commerce, the drugs are subject to destruction under 21 U.S.C. §344. *U.S.* v. *Gerovital, supra; see United States* v. *76,552 Pounds of Frog Legs*, 423 F. Supp. 329, 337 (S.D. Tex. 1976).

"The Claimants here argue that since the final destination of the drug is not within the United States, the drugs have not been introduced 'into' commerce. In support of this contention, they cite several cases which draw distinctions between the word 'into' as opposed to the words 'in,' 'from,' and 'through.' The word 'into,' however, must be read in light of the modifying words that follow. Thus, those authorities dealing with what is meant by 'into a state' or 'into a country' are inapposite. The pertinent language of the Act does not simply prohibit introduction of certain drugs 'into the United States' but rather 'into interstate commerce.' 21 U.S.C. §355(a). The Act then defines interstate commerce as 'commerce between any state or territory and any place outside thereof. . . .' 21 U.S.C. §321(b)(1). As mentioned above, 'commerce' includes interstate shipments or transportation *as such*. *Powell* v. *U.S. Cartridge Co.*, 339 U.S. 512. Therefore, the meaning of the term 'into interstate commerce' necessarily encompasses the introduction of items into the flow of shipments and transportation within the United States.

"Claimants also contend that the United States is equitably estopped from proceeding against the drugs because Claimants and others have been purchasing K.H.3 and bringing it in-bond from Europe through Texas for export for at least six years. Since the United States never proceeded against the prior shipments, Claimants claim that the United States is now estopped from proceeding against them.

"The general rule that the government is immune from the defense of equitable estoppel has, in recent years, been severely criticized and limited. *See United States* v. *Georgia Pacific Co.*, 421 F.2d 92, 99 (9th Cir. 1970). The Fifth Circuit takes the position that equitable estoppel is a proper defense against the United States only in certain situations. *United States* v. *State of Florida*, 482 F.2d 205, 209 (5th Cir. 1973), stating the test to be: 'Whether the defense of equitable estoppel may be asserted against the United States in actions instituted by it depends upon whether such actions arise out of transactions entered into in its proprietory capacity or contract relationships, or whether the actions arise out of the exercise of its power to government. The United States is not subject to an estoppel which impedes the exercise of the powers of government, *and is not estopped to deny the validity of a transaction or agreement which the law does not sanction. Sanitary Dist.* v. *The United States*, 266 U.S. 405 (1925); *Utah Power & Light Co.* v. *United States*, 243 U.S. 389 (1916). (emphasis added).' While the distinction between proprietary (private) and governmental (sovereign) function is not always an easy one to make, the Court is convinced that where as here the United States is suing to prevent violations of its laws, the United States is clearly exercising its powers of government and cannot be estopped from proceeding against the seized K.H.3.

"For the above reasons, it is therefore Ordered that the Motion for Summary Judgment by the United States be Granted and the cross-motions for summary judgment by the Claimants be Denied."

For the reasons explained in the above opinion, the court granted summary judgment to the government and ordered the article destroyed. (F.D.C. No. 62934; S. No. 80-122-315; N.J. No. 15)

Metronidazole tablets, and other specified drugs, at Brooklyn, E. Dist. N.Y.
Charged 12-12-80: when shipped by Pharmadyne Laboratories Inc., Elmwood Park, N.J., the articles were new drugs without effective approved New Drug Applications; 505(a). Default decree ordered destruction. (F.D.C. No. 63203; S. No. 80-194-186; N.J. No. 16)

MEDICAL DEVICES

X-ray control panel, Traceray III, at Louisville, W. Dist. Ky.
Charged 10-15-79: the article, which had been manufactured by Western States Supply Ltd., Pueblo, Colo., was dangerous to health when used as directed because the device would emit radiation beyond the pre-set exposure time—502(j); the accompanying labeling was false and misleading in claiming compliance with the regulation's standards, and in claiming that the device would deliver the radiation exposure stated in the instruction manual—502(a); and the article's quality fell below its purported quality—501(c).

The article was claimed by Anthony Selton (Community Medicine Foundation Inc.), Tarboro, N.C. A consent decree authorized release to the claimant for bringing into compliance. Pursuant to the conditions of the decree, the claimant obtained and filed a bond. However, the claimant was unable to bring the article into compliance within 30 days (as required by the decree) and the claimant advised FDA that it had abandoned its efforts to bring the article into compliance. Upon motion of the claimant, the bond was cancelled, the claimant was relieved of its responsibilities for compliance operations, and a U.S. marshal was ordered to retain custody of the condemned article pending issuance of an order of disposition. The government moved for an order of destruction. The court found that the claimant had failed to bring the article into compliance and accordingly ordered the article destroyed. (F.D.C. No. 62625; S. No. 79-229-221; N.J. No. 17)

X-ray control panel, Traceray III, at Miami, S. Dist. Fla.
Charged 10-10-79: the article, which had been manufactured by Western States Supply Ltd., Pueblo, Colo., was dangerous to health when used as directed because the article would emit radiation beyond the pre-set exposure time—502(j); the accompanying labeling was false and misleading in claiming compliance with the regulation's standards, and in claiming that the device would deliver the radiation exposure stated in the instruction manual—502(a); and the article's quality fell below its purported quality—501(c). Consent decree authorized release to the possessor for reconditioning. However, the article was subsequently destroyed. (F.D.C. No. 62517; S. No. 79-166-427; N.J. No. 18)

X-ray system, Traceray IV, at Pueblo, Dist. Colo.
Charged 10-2-79: the article, which had been manufactured by Western States Supply Ltd., Pueblo, Colo., was dangerous to health when used as directed because the device would emit radiation beyond the pre-set exposure time; 502(j). Default decree ordered destruction. (F.D.C. No. 62533; S. No. 79-195-670; N.J. No. 19)

X-ray system, Traceray III, at Landover, Dist. Md.
Charged 12-17-79: the article, which had been manufactured by Western States Supply Ltd., Pueblo, Colo., was dangerous to health when used as directed because the device would emit radiation beyond the pre-set exposure time—502(j); the accompanying labeling was false and misleading in claiming compliance with the regulation's standards, and in claiming that the device would deliver the radiation exposure stated in the instruction manual—502(a); and the article's quality fell below its purported quality—501(c). Default decree ordered destruction. (F.D.C. No. 62502; S. No. 79-207-186; N.J. No. 20)

X-ray systems, Traceray III, 14 seizure actions, at Dayton, S. Dist. Ohio; Greenville, S. Dist. Ohio; Dayton, S. Dist. Ohio; Mansfield, N. Dist. Ohio; Chalmette, E. Dist. La.; Rockville, S. Dist. Ind.; Muncie, S. Dist. Ind.; Washington, S. Dist. Ind.; Mt. Vernon, S. Dist. Ind.; Knightstown, S. Dist. Ind.; Bedford, S. Dist. Ind.; Wausau, W. Dist. Wis.; Spokane, E. Dist. Wash.; and Los Angeles, C. Dist. Calif.
Charged 10-23-79, 10-23-79, 10-23-79, 10-19-79, 10-1-79, 10-9-79, 10-9-79, 10-9-79, 10-9-79, 10-9-79, 10-9-79, 10-9-79, 10-19-79, and 10-9-79 (amended 10-29-79): the articles, which had been manufactured by Western States Supply Ltd., Pueblo, Colo., were dangerous to health when used as directed because the devices would emit radiation beyond the pre-set exposure time—502(j); the accompany-

ing labeling was false and misleading in claiming compliance with the regulation's standards, and in claiming that the devices would deliver the radiation exposure stated in the instruction manual—502(a); and the articles' quality fell below their purported quality—501(c). Consent decrees authorized release to owners/possessors for reconditioning. (F.D.C. Nos. 62481, 62482, 62483, 62500, 62503, 62508, 62509 62510, 62511, 62512, 62513, 62515, 62534, 62587; S. Nos. 79-216-127, 79-216-128, 79-216-130, 79-186-073, 79-171-864, 79-186-855, 79-192-008, 79-199-595, 79-199-594, 79-187-362, 79-199-596, 79-201-993, 79-152-919, 79-214-645; N. J. No. 21)

NOTICE OF JUDGMENT on Civil Penalty Action

Bucky X-ray International Inc., and **Peter A. Bucky**, New York, S. Dist. N.Y.

Charged 10-16-79 in a complaint for injunction and civil penalties: that the defendants designed, commercially promoted, sold and assembled cabinet X-ray systems used in interstate commerce for mail and package inspection and which X-ray systems are defined as "electronic products"; that when a partially assembled cabinet X-ray system identified as "Buckysearch X-ray Unit (Unit 1)" was shipped to Chicago, Ill., the X-ray system did not comply with the federal standards for X-ray systems and electronic products, since it lacked a key-actuated control, since it lacked (1)an indicator (other than milliammeters) to indicate when, and only when, X-rays were being generated and (2)an indicator (visible from each door, access panel, and port) which was legibly labeled "X-Ray ON," and since it lacked the date of manufacture permanently affixed or inscribed by means of tag or label; and proper certification that the units conformed to all applicable standards was lacking, initial reports to FDA prior to the shipment of the units were lacking, and FDA employees were not permitted to inspect documents concerning the defendants' cabinet X-ray systems; when a cabinet X-ray system identified as "Unit 2" was shipped to Hartford, Conn., the X-ray system did not comply with the same federal standards as charged against Unit 1 above and also lacked a label stating "Caution: X-Rays Produced When Energized near the x-ray controls"—42 U.S.C. 363j(a)(1) and (5), 42 U.S.C. 363j(a)(3) and (4); that the defendants had been notified they were in violation because they had not submitted specified reports; that the defendants had not notified the purchasers of the defects in the systems and had not corrected the defects; and that the defendants had failed and had refused to comply with the law.

In answering the government's complaint, the defendants demanded trial by jury; the defendants admitted the distribution of two portable, collapsible type of X-ray units to only two customers; and the defendants asserted that the distribution of such units had been discontinued, asserted that the X-ray units had been built according to federal and local standards with all protective and safety devices, with caution signs and with a warning red light when the machine was in operation; that a misunderstanding resulted when FDA investigators came unannounced to the defendants' business office; that the defendant firm had always tried to live within the regulations but that the government's maze of regulations was so vague as to be impossible to comply with, understand and interpret; that the government's cause of action was barred by the statute of limitations and, in any event, the government was guilty of laches; and that this enforcement would abridge the defendants' privileges and immunities, deprive them of property without due process of law, and deny them the equal protection of law.

The government served written interrogatories on the defendants and requested them to produce certain documents. The defendants responded to the government's written interrogatories and requests to produce documents, and also contended they were being forced to prepare the government's case by the proposed interrogatories which were overly broad and lacked specificity. The defendants contended that the action should never have been brought, and contended the action was instituted wholly and solely as a punitive measure against the individual defendant.

Ultimately, pursuant to stipulation of the parties, the defendants were ordered to make repairs and ordered to pay $1,500 in civil penalties. (Inj. No. 895; S. No. 78-104-990 et al.; N.J. No. 22)

NOTICES OF JUDGMENT on Criminal Actions

Carr Brothers Institutional Foods & Paper Co. Inc., and **Kenneth R. Carr**, president, and **James K. Carr**, general manager, Plant City, M. Dist. Fla.

Charged 4-26-82: breakfast cereal and lentil beans were held under insanitary conditions in a building accessible to rodents and were exposed to contamination by rodents; 402(a)(4). Guilty plea by corporation; $2,000 fine. Guilty pleas by individuals; $1,000 fines and 6-month probations. (F.D.C. No. 63554; S. No. 79-166-061 et al.; N.J. No. 23)

Massachusetts Coastal Seafoods Inc., Lewis Lee Harrington, president, and **Michael E. Mineo**, vice president, Magnolia, Dist. Mass.

Charged 9-16-81 by the grand jury, and superseded 10-29-81: (Count 1) while held for sale, Greenland turbot (*Reinhardtius hippoglossoides*) was repacked and relabeled in April 1977 by the placement and display of words (which were contrary to fact) consisting in part of "Carnation North Atlantic Flounder Net Wt. 16 ozs. (1 lb.) Distributed By Seabrook Foods, Inc., Great Neck, N.Y., Oceans of the World, Inc., Los Angeles, Calif." and resulting in: the indicating (by false and misleading labeling) that the Greenland turbot was flounder; the offering for sale of Greenland turbot under the name of another food, flounder; and the placing of a label which did not bear the common or usual name of the food; and (Count 2) while held for sale, Greenland turbot (*Reinhardtius hippoglossoides*) was repacked and relabeled in March 1977 by the placement and display of words (which were contrary to fact) consisting in part of "Carnation Quick Frozen Breaded Natural Fillets Flounder, Ingredients: Selected Flounder Fillets, Net Wt. 5 lbs., Seabrook Foods, Inc., Seafood Division, Great Neck, N.Y., Oceans of the World, Inc., Los Angeles, Calif.," and resulting in: the indicating (by false and misleading labeling) that Greenland turbot was flounder; the offering for sale of Greenland turbot under the name of another food, flounder; the placing of a label which did not bear the common or usual name of the food; and when shipped, with intent to defraud and mislead, to (Count 3) Seabrook, N.J., and (Count 4) Englewood, N.J., shipments of Greenland turbot, labeled in part "Carnation North Atlantic Flounder Fillets" or "Carnation Brand Flounder Fillets," were in violation of the law as above;

403(a)(1), 403(b), 403(a)(1).

The defendants pleaded not guilty and made a number of motions for discovery and inspection. With respect to such motions by each of the three defendants, request No. 1 asked the government for any and all oral, written or transcribed statements made by the defendants or of any person whose statements might legally bind the defendants, in respect to conduct constituting the offense alleged; request No. 2 asked the government for a copy of the defendants' criminal record, if any; request No. 3 asked for reports of physical or mental examinations and of scientific tests or experiments, or copies; request No. 4 asked for copies of photographs, papers, documents, photograph books, and tangible objects, within the possession, custody and control of the government, which were intended for use as evidence in chief at the trial, or were obtained from or belonged to the defendants or any co-defendants; request No. 5 asked for an inventory of all property seized by the government during the arrest of the defendants; request No. 6 asked for all available statements made by co-defendants or any alleged participants not named in the indictment which the government intended to introduce at trial and which might tend to implicate the defendants; request No. 7 asked for an inventory of all seized property which: (a)had been seized from the defendants or defendants' premises; and/or (b)had been seized from other persons or premises and which tended to implicate defendants; request No. 8 asked for copies of all government surveillance photographs taken during the investigation leading to the indictment; request No. 9 asked for the names and addresses of all government informants furnishing information either knowingly or unknowingly either before, during or after the commission of the alleged crimes; request No. 10 asked for the names and addresses of all government agents gathering information relative to the investigation of the alleged offenses; request No. 11 asked for the names, addresses, field of expertise and the substance of the testimony of any of the government's intended expert witnesses; request No. 12 asked for all criminal records, if any, of the government's trial witnesses; request No. 13 asked for the names and addresses of all witnesses who testified before the grand jury pertaining to the present indictment; and request No. 14 asked for the names and addresses of all witnesses having personal knowledge of matters alleged in the indictment and/or intended by the government to be called at the trial.

On Nov. 2, 1981, the court ruled on the motions, saying:

"Pursuant to Rule 12(d) of the Local Rules of this Court, this court takes the following action on the pretrial motions filed by the defendants:

A. Motions Filed by Defendant Harrington

"1. *Motion for Discovery and Inspection:* With respect to Request No. 1, motion allowed to the extent of any relevant written or recorded statements made by the defendant, or copies thereof, within the possession, custody, or control of the government, the existence of which is known, or by the exercise of due diligence may become known, to the attorney for the government; the substance of any oral statement the government intends to offer in evidence at trial made by the defendant whether before or after arrest in response to interrogation by any person then known to the defendant to be a government agent; and recorded testimony of the defendant before a grand jury which relates to the offense charged. In all other respects, Request No. 1 is denied.

"Request No. 2 is allowed.

"Request No. 3 is allowed.

"With respect to Request No. 4, motion allowed to the extent that the defendant may inspect, copy or photograph such exhibits and documents as the government intends to offer in its case-in-chief, or which were obtained from or belong to the defendant.

"Request No. 5 is allowed to the extent that inventories which have already been prepared and attached to a return on a search warrant shall be produced. In all other respects, Request No. 5 is denied.

"With respect to Request No. 6, to the extent that defendant seeks discovery of statements of co-defendants or co-conspirators who will be government witnesses at trial, discovery of those statements are prohibited under the express terms of the Jencks Act (18 U.S.C. 3500). . . . To the extent that defendant seeks the statements of co-conspirators and co-defendants who will not be called as government witnesses, those statements are likewise not discoverable under controlling authority. . . . Request No. 6 is accordingly denied.

"Request No. 7 is allowed to the same extent as set forth with respect to Request No. 5 above.

"Request No. 8 is allowed.

"With respect to Request No. 9, as drafted, the motion is denied. To the extent, however, that the United States is under an obligation to disclose the identity of an informant under the rationale of *United States* v. *Roviaro*, 353 U.S. 53 (1957), *United States* v. *Picard*, 464 F.2d 215 (1st Cir. 1972), and *United States* v. *Estrella*, 567 F.2d 1151 (1st Cir. 1977), the United States is hereby ordered to take all reasonable steps necessary to ensure that the informant will be available for a pre-trial interview (should defense counsel desire to interview him, and should the informant desire to be interviewed) and/or for trial (should defense counsel choose to call the informant as a defense witness). Cf. *United States* v. *Nutile*, 550 F.2d 701 (1st Cir. 1977).

"In the event that the attorney for the government cannot determine whether or not the identity of the informant must be disclosed under the circumstances of the particular case, he or she may apply to this court for an *in camera* hearing and ruling thereon.

"Requests Nos. 10 and 11 are denied.

"With respect to Request No. 12, as drafted, the motion is denied. If the United States, however, knows, or has reason to know, that any of its witnesses has a prior conviction(s), then it is incumbent upon the attorney for the government to take whatever steps that are reasonable in the circumstances in order to obtain properly authenticated copies of such convictions for use by defense counsel at trial. Such authenticated copies, however, need not be tendered to defense counsel until, and unless, the witness actually testifies at trial. Alternatively, the attorney for the government—in lieu of obtaining properly authenticated records—may stipulate at trial as to the convictions of its witnesses, if such convictions are otherwise admissible for impeachment pursuant to the provisions of Rule 609, *Federal Rules of Evidence*, or other applicable rule of law. Nothing contained herein shall be construed as requiring the Chief Probation Officer for this District to search for such records, or to make available probation records maintained by his office.

"Request No. 13 is denied.

"With respect to Request No. 14, to the extent that the motion relates to persons who will not be called as trial witnesses, motion denied. To the extent that the request relates to trial witnesses, motion denied. Even if it is proper to assume that this court has the authority to order the government to disclose the names and addresses of its witnesses (compare Conference Committee Notes, House Report No. 94-414, *United States* v. *Brown*, 535 F.2d 424, 429 (8th Cir. 1976); *United States* v. *Pelton*, 578 F.2d 701, 708 (8th Cir. 1978); *United States* v. *Krohn*, 558 F.2d 390, 394 (8th Cir.), certiorari denied, 434 U.S. 868 (1977); *United States* v. *Rogers*, 549 F.2d 490, 494 (8th Cir. 1976), certiorari denied, 431 U.S. 918 (1977); and *United States* v. *Mitchell*, 540 F.2d 1163, 1166 (3d Cir. 1976), with *United States* v. *Cannone*, 528 F.2d 296 (2d Cir. 1975)), the motion—in its present form—does not even warrant the exercise of that discretion, since defendant has only made a generalized request without any showing of need in the circumstances of this case. . . .

"2. *Motion for Disclosure of Prior Misconduct, Crimes or 'Bad Acts':* To the extent that the government intends to offer evidence of other crimes or wrongs otherwise admissible under the provisions of Rule 404(b), *Federal Rules of Evidence*, in its case-in-chief, the government shall provide the defendant, to the extent known by the government, with a generic description of the other crime or wrong, its date, and its place.

"To the extent that the government intends to offer a prior conviction under the provisions of Rule 404(b) and 803(22), *Federal Rules of Evidence*, in its case-in-chief, the government shall provide defendant with a copy of that conviction.

"In all other respects, the motion is denied.

"3. *Motion to Enlarge Time for Filing of Motion to Suppress:* Motion allowed.

"4. *Other Motions:* To the extent that this motion seeks leave to file other pretrial motions (other than a motion to suppress as set forth immediately above), motion denied without prejudice to defendant filing a motion for leave to file a specific motion(s), provided that counsel for defendant make a good and sufficient showing as to why the motions could not have been otherwise timely filed.

"To the extent that defendant seeks to join other unspecified motions (including so-called 'omnibus motions') filed by other defendants, motion denied. . . . [On motions filed by other defendants, like rulings were made]."

Subsequently, the defendants changed their pleas. Guilty plea by corporation to Counts 3 and 4; $20,000 fine. Guilty pleas by Harrington to Counts 1 and 2 and by Mineo to Counts 3 and 4; $2,000 fine each, imprisonment for one year, suspended, and probation for one year. (F.D.C. No. 61516; S. No. 77-91-535 et al.; N.J. No. 24)

NOTICES OF JUDGMENT on Injunction Actions

American Bakery & Pastry Inc., John F. Lalka, president, **John R. Lalka**, vice president, and **Ronald J. Lalka**, assistant treasurer, Detroit, E. Dist. Mich.

Charged 10-25-79 in a complaint for injunction: that the defendants at this bakery held for sale, after interstate shipment, various bakery ingredients (e.g., flour, sugar, donut mix and modified whey solids) and prepared, packed and held for sale various bakery products (e.g., cakes, bread and donuts) after interstate shipment of their components; that such bakery ingredients and products were held, prepared or packed under insanitary conditions; that some of such bakery ingredients and products contained insect filth; that FDA inspections of the defendants' bakery revealed a number of specified insanitary conditions; and that the defendants had been warned repeatedly of the insanitary conditions in their bakery; 402(a)(3), 402(a)(4).

A consent decree of permanent injunction enjoined the complained of violations, and enjoined continued operations involving interstate foods unless and until a number of specified conditions were met and unless and until all the food on hand at the defendants' bakery had been examined for filth, necessary analyses had been made, and all food shown to be contaminated was either destroyed or otherwise brought into compliance with the law. (Inj. No. 922; S. No. 79-185-482 et al.; N.J. No. 25)

Samuel Damato, t/a D'Amico's Bread Co., Worchester, Dist. Mass.

Charged 10-18-79 in a complaint for injunction: that the defendant, at his Worchester, Mass., plant, manufactured, processed and held for sale breads, rolls and pastries after interstate shipment of their components; that the defendant's flour contained insect filth; that the defendant's breads, rolls and pastries had been prepared, packed and held under insanitary conditions; that FDA inspections disclosed a number of specified insanitary conditions; that FDA analyses confirmed the insanitary conditions; and that the defendant had been warned of the insanitary conditions in his plant; 402(a)(3), 402(a)(4).

A consent decree of permanent injunction enjoined the complained of violations and enjoined manufacturing, packing, holding and distributing food which contained interstate components and which had been prepared, packed or held in the defendant's plant unless and until a number of specified methods, facilities and controls were established, operated and administered to assure that food was not contaminated and unless and until all articles of food on hand at the defendant's plant were examined for filth, necessary analyses were made by FDA, and all foods shown to be contaminated were destroyed or otherwise brought into compliance with the law. (Inj. No. 924; S. No. 78-105-644 et al.; N.J. No. 26)

Patricia A. Purcell, t/a Mid-Michigan Laboratories, Boon, W. Dist. Mich.

Charged 6-2-80 in a complaint for injunction: that the defendant manufactured, processed, packed, labeled and distributed in interstate commerce *in vitro* diagnostic products (microbiological culture media); that such products, which were devices within the meaning of 21 U.S.C. 321(h), contained microbial filth; that such products had been prepared, packed or held under insanitary conditions; that the methods used in, and the facilities and controls used for, their manufacture, packing and storage were not in conformity with good manufacturing practice; that FDA inspections revealed a number of specified deviations from good manufacturing practice regulations; and that the defendant was well aware that her activities were in violation of the law and had been warned of the deficiencies in her facility at Boon, Mich.; 501(a)(1), 501(a)(2)(A), 501(h).

A consent decree of permanent injunction enjoined the complained of violations and enjoined the production, packing, labeling or holding on the premises, and the interstate shipment of any devices (includ-

ing *in vitro* diagnostics, such as microbiological cultures media), unless and until specified methods, facilities and controls had been established, operated and administered in conformity with good manufacturing practice and all devices on hand were examined, necessary FDA tests were made, and all examined and tested devices were destroyed or otherwise brought into compliance with the law. (Inj. No. 935; S. No. 80-191-682 et al.; N.J. No. 27)

NOTICE OF JUDGMENT on Miscellaneous Action

PROven snake venom therapy and FDA regulatory letter requesting cessation of its manufacture and distribution, Miami, S. Dist. Fla.

Charged 9-26-80 by Joan F. Ripps, Faye Browning, James Yingst, Heddy Recht, Suzanne Toney (by her father James L. Toney), and Miami Serpentarium Laboratories Inc. (in an amended complaint), against the United States of America (through Department of HEW and FDA) in a complaint for injunction and declaratory judgment: that the individual plaintiffs suffered from various diseases (Joan Ripps—multiple sclerosis; Faye Browning—multiple sclerosis; James Yingst—multiple sclerosis and loss of eyesight; Heddy Recht—crippling arthritis; and Suzanne Toney—the eye disease Pars Planitis); that the treatment of multiple sclerosis, arthritis, inflammation, eye and other neurological disease with a snake venom preparation emanated from Miami Serpentarium Laboratories Inc. in 1954 to the time of this action; that it had been suggested that the venom therapy also might be effective in relieving symptoms of amyotropic, lateral sclerosis, muscular dystrophy and Parkinson's disease; that the individual plaintiffs had obtained positive results from the use of PROven (e.g., Joan Ripps—improved overall condition, remarkable transformation, immediate relief at the onset of any painful episode, improved and retained balance and coordination and restoration of hope; Faye Browning—benefits and freedom from pain and other symptoms, and partial restoration of sight; Heddy Recht—pain subsided progressively and completely; Suzanne Toney—restoration of eyesight and disappearance of cloudiness symptoms); that the Miami Serpentarium Laboratories Inc., Miami, Fla., had received a regulatory letter from FDA requesting that the firm "cease all manufacturing and distribution of PROven (or any other similar product) for use in humans"; that the government action was arbitrary, unjustified and unreasonable, and that the government action deprived them of life, liberty and pursuit of happiness as well as due process of law and equal protection under the law.

The government moved to dismiss the action or, in the alternative, for summary judgment. In response to the government's motion, the plaintiffs (assenting to the government's motion for dismissal) moved for a voluntary dismissal of the complaint because they desired to file an amended complaint so as to cure any and all defects found. (Misc. No. 619; N.J. No. 28)

Notices of Judgment are given pursuant to section 705 of the Federal Food, Drug, and Cosmetic Act. Notices of Judgment report cases involving seizure proceedings, criminal proceedings, and injunction proceedings. Seizure proceedings are civil actions taken against *goods* alleged to be in violation, and criminal and injunction proceedings are against *firms* or *individuals* charged to be responsible for violations. The cases generally involve foods, drugs, devices, or cosmetics which were alleged to be adulterated or misbranded or otherwise violative of the law when introduced into and while in interstate commerce, or while held for sale after shipment in interstate commerce.

Notices of Judgment are prepared by Food and Drug Division, Office of the General Counsel, HHS.

Published by direction of the Secretary of Health and Human Services.

Arthur Hull Hayes Jr., M.D., *Commissioner of Food and Drugs*
Washington, D.C., Nov. 1, 1982

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Section 705[375] of the Food, Drug, and Cosmetic Act: (a) The Secretary shall cause to be published from time to time reports summarizing all judgments, decrees, and court orders which have been rendered under this Act, including the nature of charge and the disposition thereof.
(b) The Secretary may also cause to be disseminated information regarding food, drugs, devices, or cosmetics in situations involving, in the opinion of the Secretary, imminent danger to health, or gross deception of the consumer. Nothing in this section shall be construed to prohibit the Secretary from collecting, reporting, and illustrating the results of the investigations of the Department.

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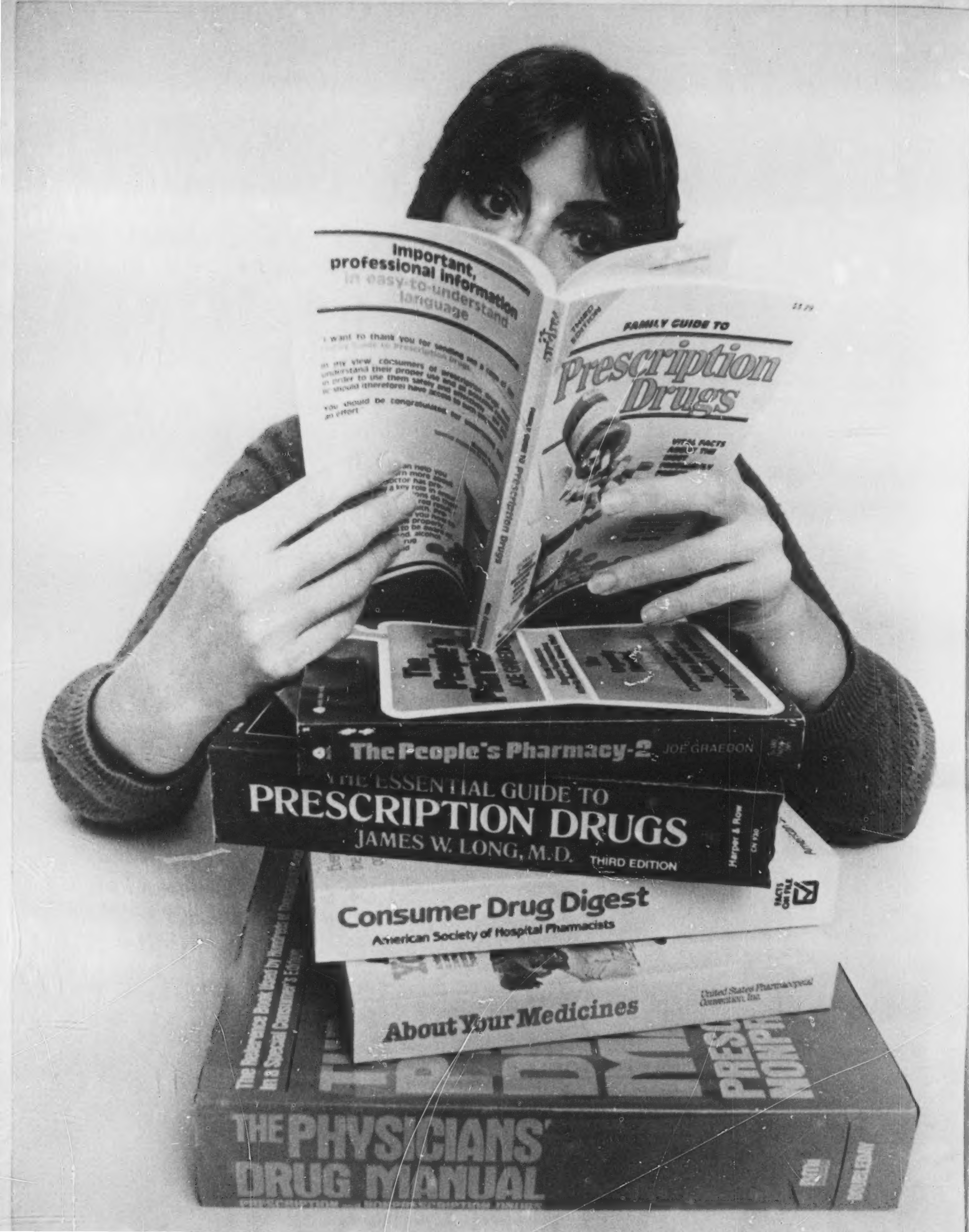
Important, professional information in easy-to-understand language
FAMILY GUIDE TO Prescription Drugs
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THE ESSENTIAL GUIDE TO PRESCRIPTION DRUGS
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Consumer Drug Digest
American Society of Hospital Pharmacists
About Your Medicines
United States Pharmacopeial Convention, Inc.
THE PHYSICIANS' DRUG MANUAL

FDA CONSUMER

VOL. 16 NO. 10 **DECEMBER 1982-JANUARY 1983**

A Physician's Spyglass for Looking Inward 4
Doctors can inspect many parts of the body's interior these days, and can identify and correct many irregularities without X-ray or incision. It's made possible by fiber optics — bundles of fine, flexible glass strands that are inserted into various body openings and transmit views of trouble spots to the doctor.

Handmade Antibodies That Go Forth and Multiply 7
Monoclonal antibodies are the offspring that result from fusing an antibody-producing white blood cell with a tumor cell. This hybrid, called a hybridoma, is painstakingly created in the laboratory. The hybrid in turn produces endless supplies of antibodies that are proving useful in diagnosis and research and may be used to treat diseases.

Of Hangovers and Love Potions 10
There's no product yet to prevent a hangover, though some will help ease the symptoms, according to an FDA advisory panel. Nor were any over-the-counter products found that would work as aphrodisiacs, or any safe or effective remedy for treating an enlarged prostate. Products for ingrown toenails, thumb sucking and upset stomach were among other areas covered in OTC panel reports.

Researchers Go For the Well-Bred Rodent 12
For biomedical research, rats or mice are usually the choice as laboratory animals. Many of the domesticated strains used today have predictable genetic characteristics, known physical attributes that make them useful in obtaining uniform test results.

Need Drug Info? You Could Look It Up 16
The growing curiosity of people about what drugs can do for them — and to them — may not be exceeded by the number of books that aim to provide this information, but there are more in print than one might think. For a little money, the consumer can get considerable information, and it's only the beginning.

All Right, Santa, Where's the Red Dye No. 2? 22
Bad candy canes sent an FDA man to the North Pole in search of the source of food adulteration. It's all told in the lead Investigators' Reports item.

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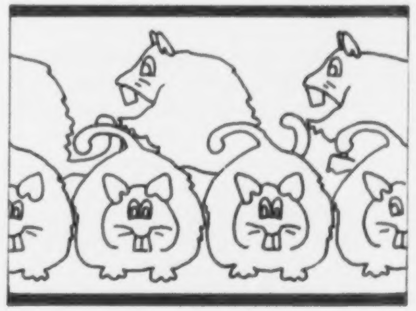


Inside Front Cover Photo (*left*):

The consumer who really wants to know all about prescription drugs has only to go to the bookstores. There's a wealth of information in a variety of books ranging from thin paperbacks to fat hard-cover volumes. What they have to say and how they say it is the subject of Need Drug Info? You Could Look It Up, *beginning on page 16.*

Reye Awareness Campaign

An article from the October issue of *FDA Consumer*, a special brochure, and a series of public service announcements for radio are the key elements in a public awareness program to alert parents that Reye syndrome, a rare but life-threatening disease, has been reported to be linked to the use of aspirin and other salicylate-containing drugs by children under 16 who have flu and chicken pox.

In addition to aspirin, many common over-the-counter and prescription drugs, including some popular cough and cold remedies, contain salicylates.

The Reye syndrome awareness campaign will enlist the help of consumer and health professional groups to circulate information to the public. The brochure, in question-and-answer format, has been sent to physicians and pharmacists who may order additional copies for their clientele. The public service announcements, recorded by Dr. C. Everett Koop, surgeon general of the U.S. Public Health Service, have been sent to all radio stations for airing before and during the flu season. A newspaper column by Dr. Koop on Reye syndrome has been made available to newspapers around the nation. In addition, reprints of the October article from this magazine, "Reye Syndrome Spells Caution to Parents," are available by writing to: FDA (HFE-88), 5600 Fishers Lane, Rockville, Md. 20857.

Salt Tablets for Contact Lenses

FDA's Office of Medical Devices has approved the marketing of 250-milligram salt tablets to be used in the heat disinfection of soft contact lenses.

Smaller FDA-approved salt tablets (135 mg) have been available for the same use but many lens wearers and eye-care professionals found the smaller tablets sometimes did not provide enough solution to rinse and heat-disinfect a pair of lenses. Thus, 250-mg tablets, though neither approved nor labeled for soft contact lens use, have outsold the approved 135-mg tablets by as much as five to one. By now approving the 250-mg tablets, FDA hopes to help assure that these products carry proper safeguards and instructions to protect patients from injury.

FDA's Ophthalmic Devices Section on May 25 recommended approval of the 250-mg tablets. The tablets approved are manufactured by Blairex Laboratories Inc., Evansville, Ind. (approved Oct. 1); Horizon Pharmacal Inc., Kansas City, Mo. (Oct. 1); Marlin Industries, Tarzana, Calif. (Oct. 4); Professional Supplies Inc., Stevens Point, Wis. (Oct. 4); Amcon Inc., Shawnee, Kan. (Oct. 5); and Ciba Vision Care, Atlanta, Ga. (Oct. 5).

The kits contain a boilable plastic mixing bottle that is large enough for only one day's supply of solution and is marked to indicate how much distilled water should be added to get the proper strength solution. Also, warnings are included in the instructions telling users to:

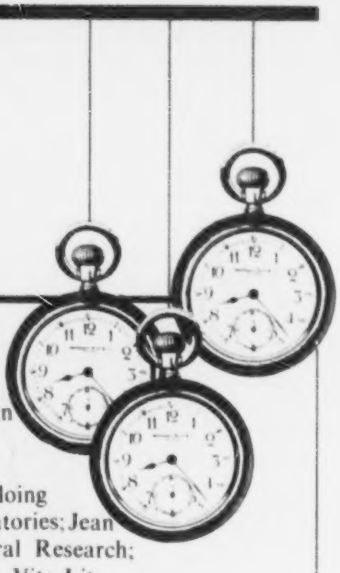
- Discard any unused solution and prepare fresh solution daily for each use.
- Use the salt solution only for heat disinfection of the lenses, not as wetting solution or eye drops.
- Use only the tablets provided in the kit to make the solutions to be used in the heat disinfection system.
- Keep the plastic bottle clean by rinsing with hot tap water before each use, shaking out the tap water and rinsing with distilled water. The bottle also should be disinfected once a week by boiling it.

FDA has found that these safeguards have helped to maintain a good safety record for the 135-mg tablets.

The manufacturers will use color coding or other methods to help users avoid mixing tablets in the wrong size bottle (e.g., mixing a 250-mg tablet in a bottle meant for 135-mg tablets, resulting in a solution that is too strong).

When soft lenses were first marketed in the United States in 1971, 250-mg salt tablets for making a solution to be used in the heat disinfection of soft contact lenses were available to consumers. But FDA was concerned that the tablets might be misused. If people failed to discard the leftover solution, for example, it could become contaminated with bacteria. Eye injury also could occur if people applied nonsterile salt water directly to their eyes as a wetting agent or eye drops. The manufacturer of the salt tablets, at FDA's request, withdrew the tablets from the market in 1978.

To replace the salt tablets, premixed sterile solutions with preservatives added to help prevent bacterial contamination were introduced. Some soft lens wearers, however, proved to be allergic to the mercury preservative in the premixed solutions. In 1979, FDA



approved several sterile, preservative-free solutions in single-use plastic bottles. Each disposable bottle contains one day's supply of disinfecting solution. While these unit-dose, preservative-free solutions avoid the potential problems of the salt tablets and the preserved solutions, they are more expensive.

Thus, in 1980 FDA approved new disinfecting kits with 135-mg salt tablets and a boilable plastic mixing bottle large enough for only one day's supply of solution. The idea was that with no leftover solution, the chances for bacterial contamination would be reduced. As with the 250-mg salt tablet kits approved this month, FDA required that the 135-mg kits contain strong warnings about the hazards of not strictly following the instructions for use.

The kits containing the 250-mg tablets approved this month differ significantly from those taken off the market in 1978 in that they incorporate these safeguards.

Starch Blockers Seized

Three days after a federal judge's ruling on starch blockers, some 7,000 bottles of the product were seized in 32 stores in the General Nutrition Center chain in the greater Chicago area.

Judge Nicholas J. Bua had ruled on Oct. 5 that starch blockers used in weight management are new drugs requiring premarket approval by the Food and Drug Administration. Judge Bua, sitting in the U.S. District Court at Chicago, also had ordered a permanent halt to further manufacture and distribution until such FDA approval—based on evidence of the product's safety and effectiveness—is granted. Ten manufacturers and distributors of starch blockers had sought in court to stop FDA from classifying the product as a drug.

Judge Bua's decision supports FDA's position, announced July 1, that starch blockers were being marketed without the necessary scientific testing to prove their safety and effectiveness as a drug. At that time, FDA informed manufacturers and distributors that they must stop marketing starch blockers. Most companies indicated their intention to comply.

However, a few firms continued to manufacture and distribute starch blockers, and a number filed suit against FDA, alleging that starch blockers are foods requiring no FDA premarket approval. Involved in the Chicago case were: Nutrilab Inc.; Naturalife-Ecovite Laboratories Inc., doing business as Paragon Laboratories; Jean Pierre Products Inc.; Natural Research; Bio-Tech Laboratories Inc.; Vita-Lite Laboratories Inc.; Dynavest; J. John Marshall, Ph.D.; J. Robert Lemmon, R.Ph.; and Ronald F. Frantz.

Another suit was filed against FDA by manufacturers and distributors of starch blockers in Federal District Court in the Southern District of New York.

In addition to seizures of starch blockers in the Chicago area, U.S. marshals, at the request of FDA and the Department of Justice, have initiated nationwide seizures of the product at the manufacturing and warehouse levels.

PCB Dump Protested

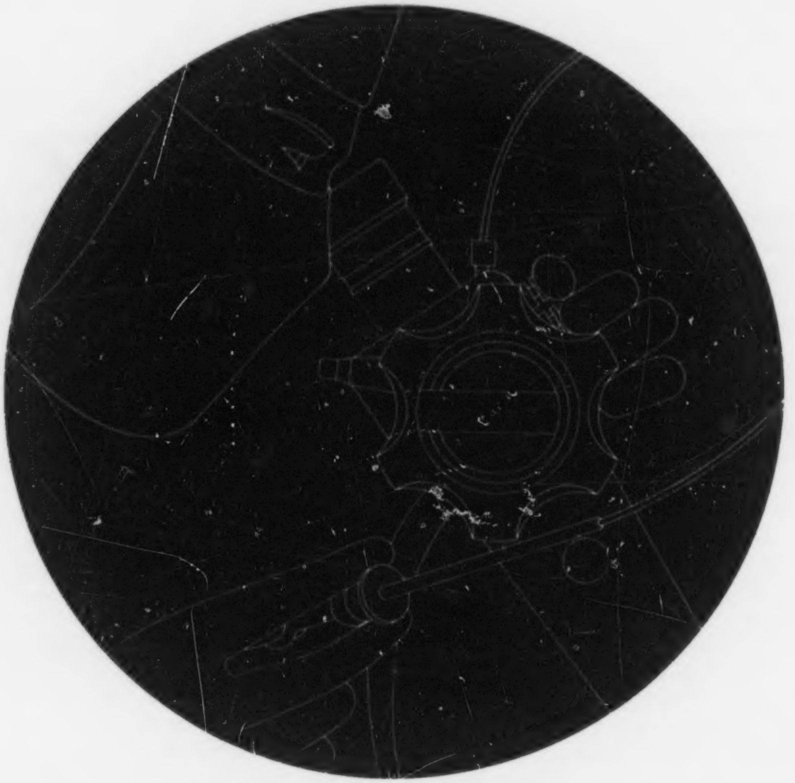
Residents of Warren County, N.C., have been demonstrating to protest the dumping of soil contaminated with PCBs (polychlorinated biphenyls) in a landfill near Afton. The soil came from 210 miles of state roadside where the PCBs were deliberately dumped in 1978. (See State Actions, *FDA Consumer*, April 1979.) Two men, one from North Carolina and one from New York, were convicted in 1981 in connection with the illegal dumping.

According to newspaper accounts, 3,500 truckloads of the tainted soil will be dumped in the landfill near the tiny rural community north of Raleigh, not far from the Virginia border. Removal of the soil from along the road was recommended by the Environmental Protection Agency. The North Carolina Department of Human Resources selected the disposal site, which was approved by EPA.

Critics charge that Warren County was chosen because its population is largely black and poor, but state officials say the site was chosen because the nature of the soil there will inhibit leaching of the chemical into the water table. Selection followed a lengthy search in several counties to find the appropriate soil conditions.

A Physician's Spyglass For Looking Inward

by Harold Hopkins



Bundles of thousands of fine, flexible, glass-coated rods or strands called fiber optics are making it possible for doctors to look deep inside ailing patients to locate and identify certain trouble spots. Then, in some cases, the doctor can deal with the problem at once—many times without an incision, without an X-ray, and with so little pain or discomfort that the patient needs only mild sedation and can remain relaxed and awake throughout. Because there's often no incision trauma and little likelihood of complications, such as infection or hemorrhage, the patient may be free to go home as soon as the procedure is over, saving money and freeing a hospital bed.

Fiber optic endoscopy (endoscopy means looking inside the body through a natural or surgically created opening) is only a little more than 20 years old and already the technology—especially for problems along the digestive tract—is fairly routine today in most medium-to-large hospitals. This means the troubled patient seldom has to go to some large metropolitan center such as New York City to get correct diagnosis and treatment. Today young gastroenterologists get training in fiber optic endoscopy when they start to specialize. Older ones already in practice go back and pick up the techniques in refresher courses.

The payoff of fiber optics, to the patient and to medicine in general, is tremendous. Not only can a doctor see just about everything that's going on in the digestive and certain other systems, by way of several of the body's cavities, but can photograph it—in color. Once the trouble is pinpointed, there are accessories or components piggy-backed onto the endoscopic unit to treat or remove diseased or suspect tissues or foreign bodies, all under the doctor's full view and control.

With their flexibility and miniaturization, as well as their amazing versatility in surgical and other therapeutic work, fiber optic endoscopes earned a place alongside the rigid endoscopic tubes that preceded them. For certain applications, flexible fiber optic endoscopes are preferable although rigid endoscopes have superior optics. In the gastrointestinal tract, rigid devices can be inserted only several inches through the mouth into the esophagus, and at most as far as the stomach for a very limited view. And the size and stiffness of the rigid devices cause considerable discomfort, and often require heavy sedation.

Fiber optic colonoscopes also can traverse the entire length of the colon, or large intestine, from the rectum. This compares to about 12 inches for rigid-tubed sigmoidoscopes.

Other procedures—such as in gynecology (laparoscope), urology (cystoscope) and orthopedics (orthoscope)—demand the capabilities of rigid endoscopes.

The qualities that make fiber optics so valuable to medicine are their capability to transmit light by internal reflections within each fiber along its entire length in the flexible bundle—even around the sharpest curves—and the adaptability of the fiber optic endoscope to the use of tubes that convey air, gas or liquids and admit surgical instruments of metal or plastic. Thus, it becomes possible for the doctor to perform several diagnostic, surgical or therapeutic functions in the same procedure, without an incision.

A skilled practitioner, using the hand controls on the outer end of the device, can manipulate the instruments on the other end just as if using the fingertips. The business end of the endoscope can be made to do a roundabout of 270 degrees to negotiate nature's circuitous disposition of the innards.

On the forward end of a gastroscope, for example, are lenses that convey to the fiber optic tips a precise, slightly magnified image of the particular area of the body's interior being examined. Each fiber then transmits a tiny bit of the image along the length of the bundle to a corresponding point on the other end at the doctor's eyepiece or the lens of a camera attached to the device.

Tubes on the endoscope serve several purposes. Liquid can be injected and suction applied to flush and clean the endoscope lens for clear viewing. Suction can remove mucus, blood, food particles and other soft materials, including bits of tissue for biopsy (a test for malignancy or other problems). Tubes can pump air or gas into the inner organs, such as stomach or intestines, to "inflate" or open them up for better viewing and a less obstructed working area.

Through tubes a doctor also can insert a wire-controlled grasping instrument, or forceps, to withdraw a bit of tissue from a suspect area for biopsy, remove a tumor that has been excised, or retrieve foreign objects such as a fishbone or a swallowed coin from the digestive tract.

Through the same tube the doctor can insert a small, thin wire noose or snare and open it to encircle an abnormal, protruding growth called a polyp, then close the noose and apply high frequency electric current through the wire as it severs the polyp at the same level as surrounding normal tissue. Heat from the electric current sears or cauterizes the stump of the excised growth to help prevent or minimize bleeding. This procedure is called a polypectomy.

The doctor, in examining the upper G.I. (gastrointestinal) tract, typically takes a half hour, sometimes more, inserting the thin, flexible black tube (a half inch or more in diameter, depending on intended use and model features) into the mouth, and onward along the esophagus and into the stomach and small intestine. The patient follows the doctor's instructions to swallow so the muscular contractions can nudge the gadget along. Scanning the food pathway, the doctor closely examines (and photographs) any part of the system that looks unusual—the esophagus (the pipe through which food is swallowed and travels to the stomach), the lining of the stomach itself, and several inches (13 to 18 centimeters) of the small intestine, which includes most of the duodenum, that troublemaker for the ulcer-prone. A tube in the endoscope can be used with a nozzle to squirt a dye into connected organs nearby—the pancreas and the gallbladder with its drainage system—connected by ducts to the duodenum (these ducts are too small to admit the endoscope head itself). Then X-rays can be used to detect tumors, gallstones and other irregularities outlined by the dye.

Endoscopy of the lower part of the digestive tract—called sigmoidoscopy or colonoscopy—takes about 45 minutes, sometimes more. The colonic endoscope, or colonoscope, is introduced by way of the rectum, permitting the doctor to examine the entire length (3 to 4½ feet, depending on the person's size and height) of the large intestine all the way to where the small intestine's last segment, the ileum, leaves off.

The most common disorders of the gastrointestinal system that can be diagnosed and sometimes treated with the aid of endoscopy are peptic ulcer, occurring mainly in the duodenum and stomach, and tumors, which can occur in any part of the G.I. system.

Peptic ulcer results when the stomach secretes the caustic acids used for digesting foods in amounts greater than needed or more frequently than needed. When peptic ulcer occurs in the stomach it's called gastric ulcer and can become cancerous. In the duodenum, it's called duodenal ulcer and it results from a spillover of excess acid into the duodenum from the stomach. Duodenal ulcers do not often become cancerous. Ulcers occur less frequently in the esophagus (from stomach backflow) and the jejunum which, with the ileum, forms the remainder (about 95 percent) of the small intestine. The acid usually is absorbed or buffered before it gets beyond the duodenum. Fortunately, then, the fiber optic endoscope can easily reach the stomach and duodenum where most of the upper G.I. trouble occurs.

Of tumors, the most common of the benign (noncancerous) kind are polyps, protruding growths that may occur in any part of the lining of the digestive tract—esophagus, stomach and the small or the large intestine, including the rectal area. Polyps may occur singly, but most often more than one occurs, and sometimes many. Although the specific cause is unknown, the tendency to develop polyps may run in families. Polyps may or may not cause trouble in the digestive tract, but doctors often recommend their removal anyway because of the possibility that they can become cancerous as they increase in size or as the person becomes older.

Malignancies can occur in any part of the G.I. tract, and early diagnosis of either cancerous or suspected precancerous growths is vital.

As weapons against these disorders, how does fiber optic endoscopy stack up against the X-ray, the other principal method of viewing inner parts of the body without incision?

Neither, of course, is perfect. X-rays subject the patient to low levels of radiation exposure, which may slightly increase the risk of cancer.

When the G.I. tract is endoscoped, the patient receives no radiation, but there is a possibility of mechanical injury ranging from irritation of the throat to hemorrhage or perforation. Perforation or bleeding of the stomach or intestinal walls from endoscopic procedures happens very infrequently, usually when surgery is being performed with the endoscope, and usually when the doctor is inexperienced in operating the device. Both bleeding and perforation are serious and the latter can result in leakage of the bacteria-laden food contents of the digestive tract into the peritoneal cavity and infection of other body systems.

X-ray is the better technique for outlining strictures (an abnormal narrowing of the intestine or stomach caused by scar tissue or tumor growth). Using a fluoroscopic X-ray, the doctor can observe the movement of barium sulfate—a harmless liquid substance impervious to X-radiation that, when sipped by the patient, shows the lower esophagus, stomach and intestines in outline. This permits the doctor to see the exact

Firsthand Scoop On The Scope

I knew vaguely that doctors had gadgets they could poke into both ends of the body for better looks, but I wasn't aware of the big leap made possible by fiber optics until I testily informed my doctor that I just wasn't going to have another X-ray series of my upper G.I. tract, as he had just recommended. (Since my original ulcer in 1951, I'd undergone what seemed to be about a dozen G.I. series—all but one negative—when doctors continued to suspect ulcer from the "nervous stomach" that had plagued me.)

"How about an endoscope?" my doctor replied. Then, as he began to explain about fiber optic endoscopy, and what he was saying sunk in, my opinion about getting my insides looked at again changed slowly from plain skepticism to delight. Well, almost.

The Frederick (Md.) Community Hospital, near where I live, is a 200-bed affair. It has a gastrointestinal endoscopic facility, and it's used by three local practicing gastroenterologists. The one chosen to view my inner works was Dr. Gerald Winnan of the gastroenterology and internal medicine firm of Miller & Winnan. Dr. Winnan is young but an experienced veteran in this new technology.

At our first session a medical history was taken of my condition and I was given a date to report to the hospital, morning or afternoon. Since they weren't letting me have food or drink of any kind after midnight on the big day, I chose morning to get it over quickly, so I could eat. "Be sure and bring someone who can drive you home afterward because you'll be taking some sedation," instructed the nurse. She gave me a printed folder on endoscopy.

At the hospital, after I was stripped down and rolled on a stretcher to the endoscopic room, no time was wasted. A "butterfly" drug dispenser was fixed to the back of my left hand and a vein pricked, through which I got a squirt or two of Valium and Demerol mixed. My throat was daubed with a local anesthetic, and we were under way. I was glad to be lying on my left side so I could see a bit of what was going on.

The end of the snake-like black scope slid down my throat with no pain at all. I was ecstatic (the sedatives working). "Swallow, please!" "Again!" Then a lot went on, though I'm unsure of the exact chronology. That Valium had a somewhat amnesiac effect on me.

The whole thing took about 30 minutes, including removal of a sample of tissue from my duodenum for biopsy, and I was trundled into recovery to snooze off the drug for about an hour. Afterward the attendant insisted on wheeling me to the curb. Hospital rules. When I stood up to get into the car, and almost lost my footing, I understood about the nurse's instructions.

A week later Dr. Winnan called me in to give me the results. I had a small ulcer, half a centimeter in diameter, shallow, no bleeding. Ought to heal up if I take four sucralfate tablets a day for three months, and avoid smoking, aspirin, alcohol, and eating things I find don't agree with me. No specific mention of coffee, but I decided to cut down on the number of cups per day. I also had a hiatal hernia, a protrusion of the stomach above the diaphragm that appears to have been responsible for some of my nausea and indi[illegible]ion, and inflammation of the an[illegible]wer) part of the stomach.

The inflammatio[illegible]dn't possibly have been picked u[illegible] X-ray. And I strongly suspect my small ulcer wouldn't have been either, because the one I had in 1951 was found only by the scars where it had healed. It was discovered years later by an X-ray.

—*Harold Hopkins*

location of detectable lesions in the system. There are some areas of the digestive system and other interior parts of the body where an endoscope cannot enter, and X-ray is the only diagnostic viewing method available.

Fiber optic facilities are costly. The equipment used for duodenoscopy or gastroendoscopy, for instance, costs a minimum of $7,500 to $8,000, and is found mostly in well equipped hospitals. It's also expensive to maintain. If water leaks into the bundle of glass fibers, as does happen, the unit must be sent away for special cleaning. Endoscopes are operated only by doctors trained in the necessary anatomy, and the procedure takes a minimum of around a half hour.

Nevertheless, fiber optic endoscopy provides some clear advantages over X-rays. Besides freedom from X-radiation (both patient and operator), it permits the taking of tissue for biopsy. This enables the assay lab to inform the doctor if the mass he has been looking at is simple scar tissue, a benign polyp or a malignancy.

Although an ulcer that has a deep sore or crater can be detected with X-rays, shallow ulcers often are missed, as are ulcers located on sharp curves or within folds or wrinkles in the stomach or intestines. An endoscope noses these out easily, and thus they can be dealt with while they're small and less likely to mean Big Trouble.

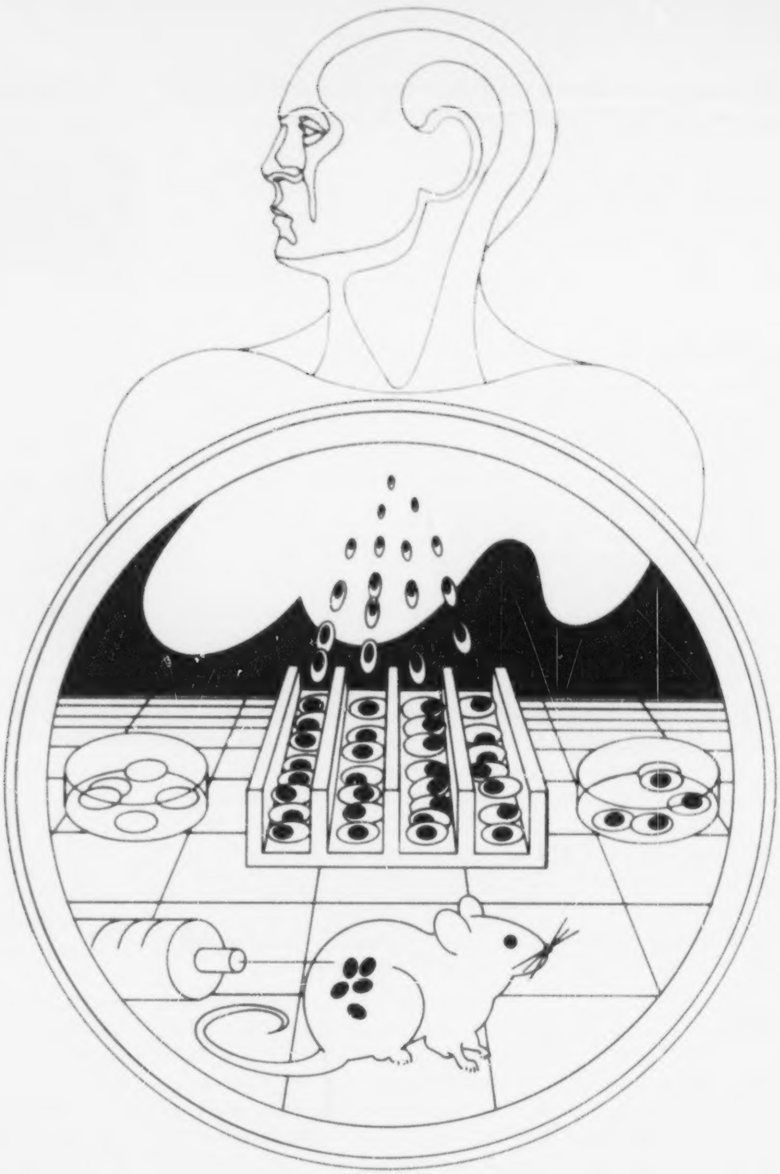
With endoscopy a doctor can detect inflammation by observing discoloration, and can instantly evaluate the extent and degree of the inflammation and photograph it for comparison with previous or future examinations. X-rays permit none of these advantages.

The flexible fiber optics of today were invented and perfected into a practical diagnostic instrument in 1956-57 at the University of Michigan at Ann Arbor. They consist of optical glass and glass of lower refractive index melted and drawn so as to make a composite, insulated strand. Fiber optic endoscopy is relatively new, and significant advances and refinements are still being made, especially in Japan, Germany and the United States. Currently the trend is toward reducing the diameter of the endoscope to make it easier for the patient to swallow or otherwise tolerate, and to adapt it better for examination of various body systems.

But the main direction of today's endoscopic application research is toward additional or improved therapeutic or surgical functions. Researchers would like to perfect endoscopes less likely to cause bleeding or lesions during use or that promise more safety in removing polyps. The endoscope is eminently adaptable to laser surgery, since the fiber optics will transmit laser beams. Endoscopic refinements may allow perfection of the technique of removing gallstones and other blockages of the bile duct to permit drainage that will relieve the jaundice resulting from blockage of this canal.

Harold Hopkins is editorial director of FDA Consumer.

Handmade Antibodies That Go Forth And Multiply



by Annabel Hecht

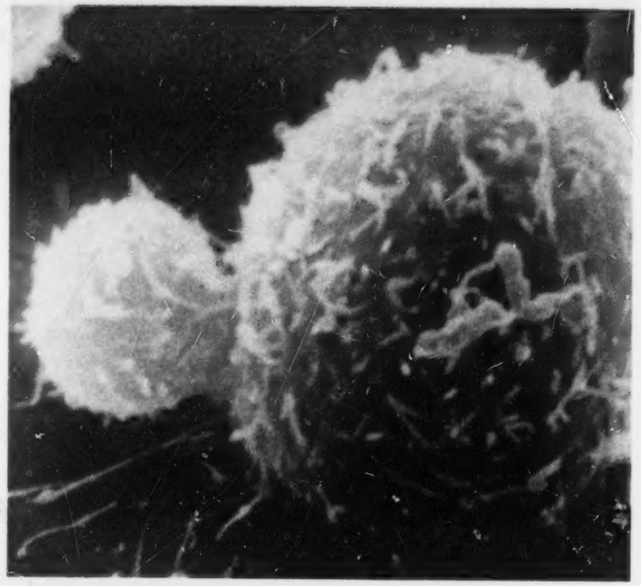
Guided missiles, magic bullets or SMART biological bombs—whatever they may be called, monoclonal antibodies are the hottest new technology on the biomedical scene today. Born of hybridomas—hybrid cells of mixed parentage—monoclonal antibodies already have shown themselves to be valuable as laboratory diagnostic and research tools and, in time, may play a key role in treating cancer and other diseases.

There's nothing new about antibodies themselves, since they are a natural part of the body's immune system. Antibodies are large protein molecules produced by lymphoid (white blood) cells in the spleen or lymph nodes. They are produced when the body is invaded by foreign substances such as viruses or bacteria. These invaders carry distinctive components called antigens. When the body is attacked, antibodies enter the bloodstream and attach themselves to the antigens on the invaders, thus tagging them so they can be destroyed by other, scavenger cells. After the invader has been neutralized, the antibodies remain in the blood. The next time that particular antigen-bearing molecule invades, the body's defenses are already mobilized.

This is the process that makes vaccines work. The body is induced to produce antibodies against specific diseases by injections of weakened or killed bacteria or viruses, thus making the individual immune to the real disease when exposed.

Antibodies also have an important job outside of the body. Blood serum containing antibodies is used for such diverse purposes as matching donors and recipients in organ transplantation, identifying strains of infectious viruses, blood group typing, and measuring the amount of substances such as hormones, toxins or viral antigens in a patient's blood or other body fluids.

Much of the blood serum used in these laboratory tests comes from animals, but there is a major drawback to this source of serum. What comes out is not a pure product. When



This remarkable scanning electron micrograph shows the actual fusion of a lymphocyte and myeloma cell. The myeloma is the larger of the two cells. Photograph courtesy of Hybritech Inc., La Jolla, Calif.

an animal is injected with an immunizing agent its blood will contain a complex mixture of antibodies, some against important antigens in the injected substance, some against minor contaminants, plus many others the animal produced in response to previous exposure to other immunizing agents. To complicate things further, the same agent may produce a different mix in a different animal. This makes it difficult to standardize laboratory tests using antibodies from blood serum.

For many years scientists sought a way out of this predicament by looking for a way to produce large amounts of very specific and very pure antibodies.

Enter the hybridoma and its offspring, the monoclonal antibody.

A hybridoma is a combination of two types of cell. One is an antibody-producing white blood cell and the other is a tumor cell, called a myeloma, that has the enviable ability to reproduce itself endlessly. The name "hybridoma" comes from the combination of "hybrid" plus "myeloma."

The technique for creating hybridomas was discovered in 1975 in England at the Medical Research Council's Laboratory of Molecular Biology in Cambridge. Here Cesar Milstein and Georges Kohler learned it was possible to fuse the two types of cell to produce a hybrid with the antibody-producing capacity of the white blood cell and the immortality of the tumor cell. From this marriage comes a single cell that can be cloned to produce an endless supply of a single antibody. Hence, the monoclonal antibody.

The process begins with injection of a specific antigen into a mouse whose spleen then starts producing the white cells that will make the desired antibody. The mouse's spleen is removed and the white cells harvested. These cells and myeloma cells are fused with the help of a chemical, usually polyethylene glycol. That's the easy part.

The process leading to the cloning of the hybridomas takes a bit longer—two, three or four months longer.

The first step is to select the right cell for cloning. Initially, several thousand pairs of cells undergo the fusion procedure, but only a few will produce the desired antibody. To narrow the field, the collective hybrid cells are distributed in multi-well culture dishes, plastic containers usually with 96 indentations or wells. The contents of the wells are then monitored and assayed to eliminate cells that didn't fuse and those containing nonsecreting cells called "silent companions." This process may have to be repeated many times before the desired cell or cells can be isolated.

A more sophisticated, more expensive, way of selecting the desired hybridoma involves use of a fluorescence-activated cell sorter, an elegant laser-based device that sorts cells according to characteristic markers on their surface.

Once the desired hybridoma has been isolated it can be mass produced, by growing it in a culture medium, thus providing a constant supply of identical cells that secrete an endless supply of identical antibodies. Hybridomas also can be frozen and stored for later use. Most hybridomas used today claim mouse cells as their parents. About two years ago scientists learned it is technically possible to make hybridomas using lymphoid cells from human blood.

Because of their purity— or "exquisite specificity," as some scientists describe it—monoclonal antibodies are being widely used in immunological research. For the first time, scientists are able to study the antibody-antigen reaction at the chemical level. They are using the new hybrid-derived antibodies to learn more about the surface of normal and diseased cells. And they are able to identify subpopulations of human lymphocytes, blood cells that are essential to the body's immune responses. With their unique ability to detect minute differences in viruses, monoclonal antibodies are proving valuable tools in understanding how the influenza virus changes its protein coat from year to year, thus eluding the protective power of vaccines.

Monoclonal antibodies also have become laboratory aids, having been incorporated into systems used to purify interferon, the elusive disease-fighting component of white blood cells.

What is perhaps most exciting will be the clinical applications of monoclonal antibodies in the diagnosis and treatment of human disease. Products in these areas will be, and in fact already are being, regulated by the Food and Drug Administration. Regulatory responsibility is shared by two centers. Laboratory diagnostic tests are under the purview of the newly created National Center for Devices and Radiological Health, while all injectable monoclonal antibody-containing products as well as a small group of blood bank-related *in vitro* diagnostic products come under the Office of Biologics in the National Center for Drugs and Biologics (also newly created).

The medical device staff already has approved a number of laboratory diagnostic devices incorporating monoclonal antibodies, including a test for pregnancy and one to assess certain types of allergies. Several newly approved diagnostic tests are designed to aid in the detection of various types of tumors, such as prostatic and colorectal tumors.

A laboratory test using monoclonal antibodies to detect the presence of rabies virus in tissue samples also has been approved, as have several tests to measure levels of thyroid hormones, human growth hormones or prolactin in blood samples. Such tests will aid in the diagnosis of thyroid conditions, pituitary abnormalities, or problems related to hormonal mechanisms in human milk production.

Monoclonal antibodies specific for gonococcal antigen (the bacteria causing gonorrhea) are now part of new laboratory tests for the rapid diagnosis of this disease. And new hybrid-born antibodies are included in a diagnostic device that gives a precise count of the body's T cells, a type of white blood cell. This provides a performance measurement of the body's immune system.

In the area of blood bank diagnostics, the Office of Biologics has already licensed three different anti-human globulin reagent-type products containing monoclonal antibodies. These are used to determine whether a patient has hemolytic anemia and also to detect harmful antibodies in the donor's blood. One of these diagnostics was, in fact, the first FDA approved monoclonal antibody product.

No injectable monoclonal antibody products have been approved as yet, but it is estimated that by the end of the decade at least a dozen may be available for diagnostic and therapeutic use.

Research scientists have already developed antibodies to specific antigens associated with cancer of the lung, breast, colon and pancreas and melanoma, a type of skin cancer. It may not be too long before these special antibodies will be aiding in the detection of cancer that can't be identified with current diagnostic methods. The antibody will be tagged with a radioactive material, injected into the patient, and followed with a scanning device while it homes in on the cancer site.

Research also is under way on the use of monoclonal antibodies in the treatment of cancer. In this case the antibodies will serve as a vehicle to carry selected cancer drugs directly to the tumor without harming the surrounding, normal tissue. Unfortunately, nature has put some roadblocks in this avenue of research. It seems there is virtually no tumor-specific antigen—that is, one that is found only on one type of tumor and nowhere else. To further confuse matters, tumor cells apparently can "turn off" or fail to secrete the antigen the monoclonal antibody is seeking. What this means is that a great deal more research must be done before such a treatment will be ready for FDA approval.

Monoclonal antibodies can be produced that react with certain organs, tissues or cell types. Human monoclonal antibodies may one day replace current sources of Rh immune globulin, used to prevent Rh incompatibility disease in newborn infants. At the present time, sensitized women who have just given birth provide the main source of plasma used for manufacture of Rh immune globulin.

Another potential use of monoclonal antibodies may be to thwart the immune system by blocking the antigen that causes the body to reject organ transplants.

Also in the future there is the possibility that antibodies produced from human hybridomas may be injected into patients to neutralize potentially toxic drugs such as digoxin, a heart drug for which there is a very narrow margin between a safe dose and a dangerous one.

Immune globulin products (such as tetanus immune globulin), which are made from human blood plasma, have been available for many years. Now that it has been shown that hybridomas can be made from human blood cells, it is entirely possible that highly potent monoclonal human antibodies will be tailor-made to treat a variety of bacterial, viral, mycoplasmal, fungal or parasitic diseases. Monoclonal human antibodies also may be developed against certain allergy-causing substances and possibly even against reptile and insect venoms.

At this time, FDA's approval of monoclonal antibody-containing products can't be done by the book. Because of the newness of the technology, that book hasn't been written. This means that each application must be dealt with individually.

In the Center for Devices and Radiological Health, regulatory concerns center on the product's performance, or how a product compares with similar products already on the market. What is important is that each product's safety and effectiveness can be validated scientifically.

Regulatory concerns for *in vitro* blood bank diagnostic products are similar. Specificity, sensitivity, stability, potency and consistency must be demonstrated, and the product standards for the particular blood bank diagnostic group they represent must be met before a new monoclonal product will be licensed by the Office of Biologics.

Injectable monoclonal products will present new and different problems. Some involve complications in manufacture, such as maintaining lot-to-lot uniformity of the product. While it is rare, mutations have been known to develop in a hybridoma cell line. Then there are problems that might develop during clinical testing, such as the potential hazard of allergic reactions following repeated administration of the monoclonal antibody. Cross reactions with blood or tissue antigens also have been reported.

Another major concern is the possibility that contaminants, such as a hitchhiking virus, might be cloned along with the hybridoma. All of these problems are being anticipated in the Office of Biologics well before the first monoclonal injectable product comes down the line.

The new hybridoma technology is still in its infancy but already many new firms have been formed and existing companies are gearing up to bring to the market new products containing the remarkable monoclonal antibodies. It is estimated that the market for these products, which will have industrial as well as medical uses, will reach the billion dollar range during this decade. All of which suggests that hybridomas and their monoclonal offspring will live up to their promise as a "revolution" in biotechnology.

Annabel Hecht is a member of FDA's publications staff.

Of Hangovers And Love Potions

Much as the average consumer would like it to be otherwise, there just isn't a drug, prescription or over-the-counter, for every ache and pain or medical condition. There are, for example, some products that will relieve the symptoms that follow overindulgence in food and drink, but not a thing that will prevent a hangover. So says an advisory panel of nongovernment experts, one of 17 such groups that are reviewing for the Food and Drug Administration the effectiveness of over-the-counter (OTC) drug products.

The Advisory Review Panel on OTC Miscellaneous Internal Drug Products drew the conclusions on overindulging. Its report was one of a number of documents recently published by FDA. Some are new panel recommendations; others are tentative final monographs that represent FDA's decisions regarding ingredients and labeling of specific drug categories. One is a final rule. Following is a rundown of the publications:

NEW REPORTS

Upset Stomachs

Bismuth subsalicylate and sodium citrate in solution are safe and effective for use in relieving symptoms of upset stomach due to overindulgence in the combination of food and drink, according to the miscellaneous internal drug panel. These symptoms usually consist of nausea, heartburn and a feeling of fullness, though other symptoms also may be present, the panel noted.

These products may be labeled, "For the relief of upset stomach due to overindulgence in the combination of food and drink," but they can't claim to provide "fast relief" or "quick relief."

Hangover Products

The word "hangover" is commonly used to describe noxious feelings encountered several hours after the sporadic ingestion of large amounts of alcohol. The panel said that a hangover remedy would be considered safe and effective if it contained a combination of ingredients from two or more of the following categories: analgesics (painkillers), antacids and caffeine. Although the panel on analgesic and anti-rheumatic drugs recommended against combining aspirin and an antacid for gastric distress, the miscellaneous internal drug product panel felt the combination is acceptable as long as the final dosage form at least meets the buffering capacity required of an antacid.

Labeling for hangover remedies should include all of the symptoms the active ingredients in the product would normally be expected to relieve, said the panel. Claims related to the speed of action (fast relief, quick relief) were ruled out.

Anyone who is looking for a drug that will prevent inebriation is out of luck. The panel said there are no safe and effective ingredients for this purpose. Fructose may be safe in minimizing inebriation but more study is needed to establish its effectiveness. The same is true of activated charcoal; it will not prevent a hangover. Activated charcoal may be safe but more study is needed to establish its effectiveness.

If any ingredients prove effective, product labels shouldn't be allowed to say a product will prevent inebriation or the symptoms of hangover, the panel said. What labels can say is that the product will minimize these conditions.

Aphrodisiacs

The panel on miscellaneous internal drugs also looked at a category of OTC ingredients that might seem an unlikely candidate for an FDA review—aphrodisiacs. The panel examined a number of exotic-sounding ingredients, including gotu kola, ginseng, licorice, sarsaparilla, cantharides (Spanish Fly), nux vomica, Pega Palo, strychnine and yohimbine, along with the hormones testosterone and methyltestosterone. There is no substantive evidence whatever to support the claims of aphrodisiac action attributed to these ingredients, the panel said. Such claims have been transmitted largely through folklore and exploited by manufacturers who prey on the gullibility of people who most likely are in need of counsel or therapy.

Furthermore, the panel said, all labeling claims for OTC aphrodisiacs are false, misleading or unsupported by scientific evidence.

No Prostate Relief

In a third report from the Panel on Miscellaneous Internal Drug Products, three ingredients—glycine, alanine and glutamic acid—used to treat symptoms of benign prostatic hypertrophy (enlarged prostate gland) were classified as not safe or effective. The condition is not a self-diagnosable disorder, and OTC treatment might unnecessarily delay diagnosis and treatment of a prostatic malignancy, the panel said.

Those three new reports of the miscellaneous internal drug panel were published in the Oct. 1, 1982, *Federal Register* by FDA to obtain public comments on the panel's recommendations. Final standards for ingredients and labeling for these categories of drugs will be published after the agency has evaluated the panel reports and the public comments.

TENTATIVE FINAL MONOGRAPHS

The next to last step before a final standard is issued for an OTC drug category is publication of what is called a "tentative final monograph." This is the point at which FDA makes its own position known.

On Sept. 3, 1982, four tentative final monographs were issued in which the agency tentatively adopted recommendations of the Advisory Review Panel on OTC Miscellaneous External Drug Products. The panel had said:

- Denatonium benzoate at 0.35 percent or less and sucrose octaacetate at 6 percent or less are safe, but there are insufficient data to establish their effectiveness as *nail-biting* and *thumb-sucking* deterrents.
- Hydroquinone in concentrations of 1.5 to 2 percent is a safe and effective *skin-bleaching agent* or skin lightener.
- Salicylic acid in concentrations of 5 to 17 percent in a collodion vehicle is acceptable as a *wart remover*.
- Sodium sulfide to 1 percent and tannic acid to 25 percent are safe, but there are insufficient data to establish effectiveness for *ingrown toenail* relief.

FDA also made some minor changes in the recommended labeling for these products. (The original panel reports were discussed in "Relief for Warts; None for Nail-Biters" in the February 1981 *FDA Consumer* (page 13), and in "Sunscreens Aid Users of Skin Bleaches" in the June 1978 issue on page 23.)

After public comments on the tentative final monographs are evaluated, FDA will issue final monographs, which will become effective 12 months after their publication in the *Federal Register*.

FINAL RULE

Camphorated Oil Products

Camphorated oil, or any drug product containing camphor in oil, or any other drug product containing camphor that is represented, suggested or purported to be camphorated oil, such as "camphor liniment," "camphor oil" or "camphorated liniment," have been declared misbranded and not safe for human use, according to a final rule published by FDA in the Sept. 21, 1982, *Federal Register*. This means that such products can no longer be marketed.

The agency's decision was based on the recommendation of the Miscellaneous External Drug Products Panel. Because of the risk to public health posed by the potential for accidental ingestion of camphorated oil drug products, FDA did not follow the full OTC drug rulemaking procedure, but went directly to a final rule after consideration of comments on the panel's original proposal. Ingesting camphorated oil can cause death, mental retardation or convulsions.

—Annabel Hecht

Researchers Go For The Well-Bred Rodent

by John J. McKeon

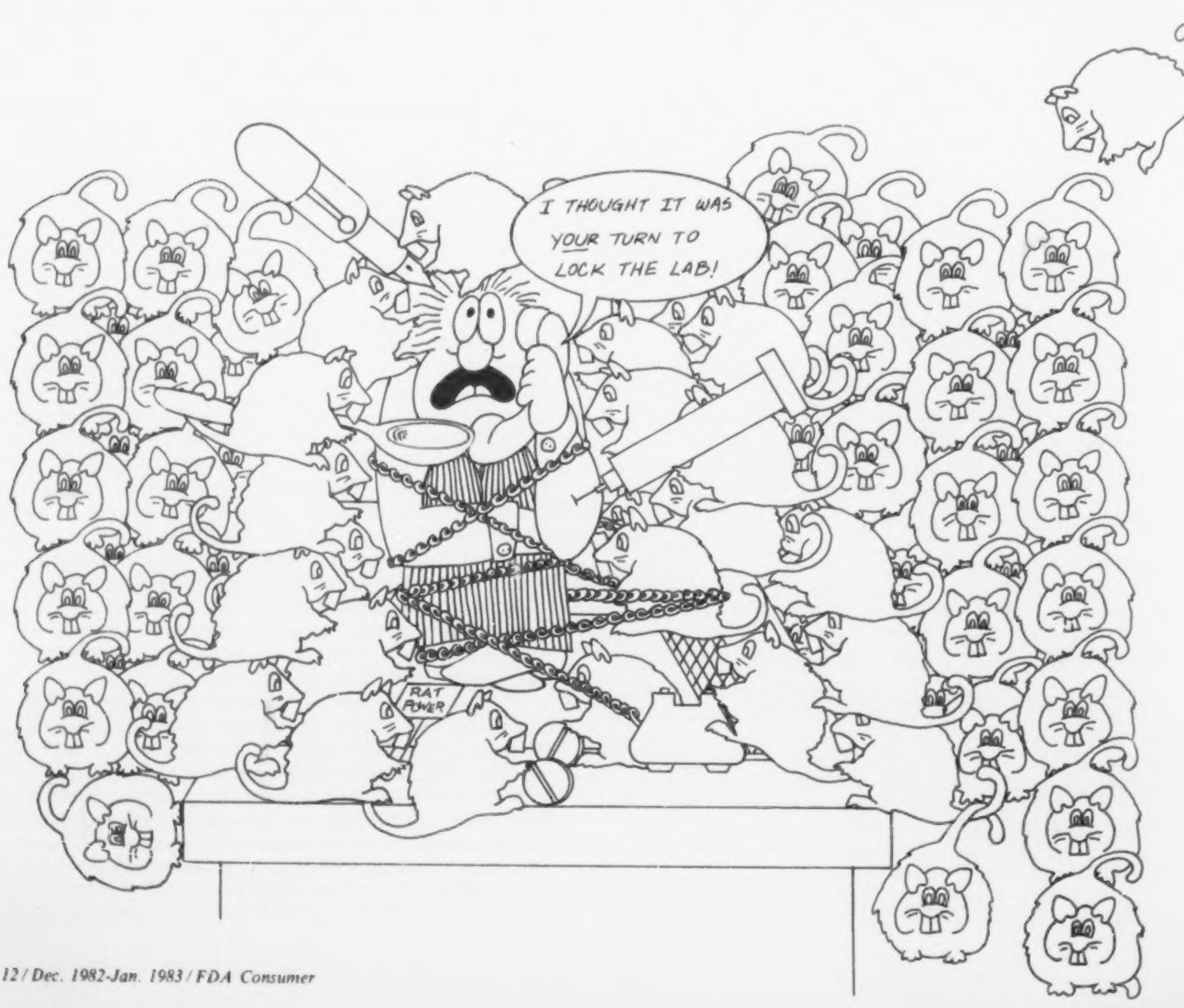
“Men died without attendants and were buried without priests. The father did not visit his son, nor the son his father. Charity was dead and hope crushed.” So wrote the French physician Guy de Chauriac of the Black Death, the plague that swept over Europe in the middle of the 14th century, carried by the same Norway rat which today has become one of mankind's most valuable allies in research to promote health and save lives.

It's a nice irony that humans for centuries have fought to eradicate rats and mice as notorious spreaders of filth and economic depredation. Yet scientists have been working intensely for considerably more than a hundred years to turn first the common alley rat, *Rattus norvegicus*, and later the common house mouse, *Mus musculus*, into the most practical and plentiful experimental animals available for biomedical research today. Special domesticated forms of these animals have come to occupy such a fundamental place in the laboratory that it's hard to imagine how some modern research could go on without them.

Look into any major biomedical science endeavor, from cancer research to product safety, from drug development to gerontology, and you'll find these adaptable animals. Estimates of the combined total number of rodents used annually are difficult. But most guesses exceed 20 million.

A 1978 trade estimate put the totals of rodents acquired by users at 13,400,000 mice and 4,360,000 rats. Some of these no doubt were used to start colonies or to supplement existing ones.

For makers of consumer products, from cosmetics to soft drinks, armies of


I THOUGHT IT WAS YOUR TURN TO LOCK THE LAB!
RAT POWER

mice and rats provide the first clues when a product might hurt as well as help, or when an ingredient—for example, the well-publicized saccharin—poses a potential hazard. The pharmaceutical industry uses rats in large numbers to establish effective doses, measure dosages that may cause adverse side effects, and produce results that need further study before a drug is marketed. Scientists have induced tumors in rats and mice to study their characteristics and seek out ways to control or destroy them. Rats are teaching us how we learn and how we respond to stressful environments. Every day, millions of rats and mice give scientists a big assist in making tomorrow's life better and safer for everyone.

Today's laboratory rodent is a far cry from the vermin of yesteryear. Its breeding is monitored by sophisticated computers and its lineage can be traced, in some cases, through hundreds of generations. Its genetic background is known in enormous detail. It is sometimes bred randomly with others of the same type, sometimes mated only with those in the same litter. It can be bred to have a wide range of normally occurring characteristics, or to be very special indeed.

Rats and mice are widely used instead of larger animals for a variety of reasons. They're less expensive than most animals, and it can be cheaper and easier to maintain a large colony of mice or rats—to house them, feed them, handle them and clean up after them—than to maintain a similar colony of larger animals.

They also begin breeding within a matter of weeks after birth and have large litters that provide a cross-section of several generations of animals in a relatively short time. If one imagines the relative difficulty of studying chemically induced birth defects over four generations of mice and over four generations of chimps, the rodent's advantage becomes clear.

One of the biggest advantages is that today's common strains of mice and rats are among the most exhaustively studied of animals. Dealing with a commonly used strain of mice such as the BALB/c, a scientist can ascertain much of the animal's past, its present genetic makeup, and any interesting conditions ever noted by other researchers. An investigator at Harvard University, using a specific substrain of BALB/c mice, can read a published paper from a colleague at UCLA who used the same substrain and assume with high confidence that they're both using the same animal.

The researcher using a larger animal such as a primate must deal with animals often caught in the wild, or those only a few generations removed from the wild. Their lineage is largely unknown.

The point, of course, is that when inbreds are used, variations from animal to animal are nearly eliminated as a possible factor affecting results from an experiment. When something unexpected happens, such as an unforeseen tumor, the investigator can delve back into the animal's past to find if that tumor has ever been encountered in that substrain before, and the conditions and circumstances involved.

Although animal breeding has grown more sophisticated along with the broader use of computers and the growth in fundamental genetic knowledge over the last 25 to 30 years, rats and mice were being carefully bred for the lab long before we knew anything about either data processing or DNA.

One epochal event occurred in 1906, when Dr. H. H. Donaldson left his position as dean of the Ogden School of Science at the University of Chicago to be professor of neurology and director of research at the Wistar Institute in Philadelphia. Dr. Donaldson brought with him a colleague, Dr. Shinkishi Hatai, four pairs of albino rats, and a growing conviction that the rat was a nearly ideal experimental subject.

At Wistar, Donaldson and his colleagues launched a huge interdisciplinary research program, probing exhaustively into the rats' growth patterns, anatomical characteristics, conditions that affect nervous systems, and many other features. Donaldson published nearly 100 papers and books over the next three decades, including *The Rat: Data and Reference Tables for the Albino Rat and the Norway Rat*. This book, published in 1915 and updated in 1924, is an encyclopedia of the rat, containing 469 pages of text, 212 tables, 72 charts and more than

2,000 references.

In 1909 Wistar scientists began inbreeding the albino rats descended from Donaldson's first four pairs, and by 1920 these rats were divided into two separate lines, each of which had reached generation 38 of brother/sister mating.

The Wistar staff also pioneered in developing cages, diets, breeding techniques, and other practices that contributed to the success of the albino rat in the lab. Even the Wistar Colony Building that opened in 1922 was innovative: It was an early application of the concept of cleanliness in an animal facility.

It was with Wistar-bred female rats that Robert W. Dawley, about 1925, started the new line he called Sprague-Dawley. Over the years, rats from the Wistar colony contributed significantly to the formation of many other lines.

The number of rodents used in laboratories in the United States is reported to be declining each year—not spectacularly, but slowly and steadily. Among the principal reasons mentioned for the decline: the availability of non-animal alternatives for some tests (though relatively few), economic considerations that have tended to reduce studies to the most essential ones, and the improved quality of today's mouse and today's rat. The improved quality of modern rodents is such that consistent and accurate experimental results often can be obtained with fewer animals than before.

A certain percentage of all rats, for instance, will have diabetes, in a form very similar to that which afflicts humans. Whereas the researcher once had to study enormous populations to obtain relatively few diabetic rats, today he or she can order all the diabetic rats needed.

Filling the researcher's needs for laboratory animals of all kinds, however esoteric, has become the focus of an industry estimated at $230 million worldwide (the estimated total world market for laboratory animals other than primates, excluding the Soviet Union and the People's Republic of China).

By far, the majority of all the rodents purchased and used by American scientists are what might be termed ordinary. The Charles River Breeding Laboratories in Massachusetts, for example, can provide a hairless mouse lacking a thymus gland, but sells only about 15,000 of these nude mice a year, compared to some 3.5 million plain, outbred mice. A limited number of strains of both rats and mice accounts for the bulk of all usage.

But even the ordinary rodent is a product of extraordinary breeding techniques.

Rodents can be either heterozygous or homozygous. Heterozygous animals are those that result from the random mating of individuals to others of the same strain. In theory, this technique produces an even distribution of traits through the population in something resembling "normal" patterns of occurrence. There will be occasional expressions of recessive genetic characteristics, as would happen in any large population, but upon extensive observation, these, too, become predictable. They become part of the individual rat's or mouse's scientific profile.

Homozygous animals are the offspring of mating between littermates, or of a male with females he has fathered. The intent is to produce whole populations that are identical twins of each other. The intrusion of new, unwanted genes into a stable gene pool is minimized, if not entirely eliminated. Over a sufficient number of generations even the rarest of recessive traits can be bred out of the animals—or can be fixed by inbreeding until a rare fluke becomes a 100 percent occurrence. An inbred rodent stock is regarded as "controlled" after 20 generations of brother/sister mating.

Those generations pass quickly. Rats are ready for mating when about 10 to 14 weeks old, take 21 to 22 days for gestation, and have litters of 6 to 20 young. The female is ready for mating again almost immediately after giving birth.

Mice show similar patterns: a minimum breeding age of 7 to 10 weeks,

20 to 21 days gestation, litters of 6 to 14.

A number of techniques are used to estimate when conception occurs. Breeders take vaginal smears from female rats and inspect the droppings pan under the cage daily for "plugs" that are often discharged after mating. Mice do not usually drop these plugs and a careful visual inspection of the female is necessary. A high degree of accuracy can be brought to estimating when to expect birth.

Females have a long potential breeding life. A few may be mated only once. For example, when germ-free offspring are desired, the young may be removed from the mother by surgical methods, to protect the fetuses from exposure during passage through the birth canal.

The largest commercial breeders often deliver and raise all their animals in controlled environments, whether or not the customer demands it. The goal is to provide the researcher with as perfect a specimen as possible—with no unwanted viruses, parasites or bacterial infections.

Breeders can produce animals in four degrees of freedom from microorganisms.

Axenic animals have no microorganisms in their systems at all, at least none detectable. To maintain that freedom they must be very strictly isolated from microorganisms throughout their lives.

Defined Flora animals start out completely free from microorganisms and then specific bacterial flora are introduced into their bodies. To keep conditions stable within their bodies, these too must be isolated.

Specific Pathogen Free (SPF) animals are described according to what's missing from their systems. A rat may harbor all of the normally occurring microorganisms except one, and thus may present a fine opportunity for study of the role of that particular microorganism. To prevent the undesired pathogen from reappearing, isolation is once again desirable.

Conventional rats and mice are those that are not covered in the foregoing categories and which normally have a less controlled biological flora.

The cost of a common outbred mouse runs about $1 and increases to $8 or $9 for mice bred for special purposes. Similarly, rats cost about $3.50 apiece on the low end and the price rises to about $15 for special animals. Some of the better-known rat strains are the Sprague-Dawley, Osborne-Mendel and Fisher 344. Of the hundreds of mouse strains, some of the more commonly used inbred mice are the BALB/c, the C3H, the C57BL/6, the A, and the CBA.

A majority of today's research calls for rodents that are genetically uniform, though not necessarily inbred. But there is a growing demand for inbred animals, and this demand reflects some trends in the scientific community.

One example of a "hot" research area today that demands homozygous animals is the broad field known collectively as monoclonal antibodies (see "Handmade Antibodies That Go Forth and Multiply," page 7, this issue).

Precision and accuracy in monoclonal antibody work demands a test animal from which every possible genetic "quirk" has been bred out. At present, one of the animals of choice for this work is the inbred mouse known as BALB/c.

From consumer product safety to the leading edge of cancer research, it would be hard to think of a key research area that doesn't owe an enormous debt to today's carefully bred rats and mice. Their suitability to a broad range of tests, together with the economy and the high sophistication of their breeding, have helped make rodents indispensable in laboratories all over America. Although no laboratory animal is ideal, it's likely, as both genetic knowledge and breeding techniques improve, that the rodent will become as near to perfect as a laboratory subject can be.

John J. McKeon is a freelance writer.

Need Drug Info? You Could Look It Up

by Egon Weck

Family Guide to Prescription Drugs
Consumer Drug Digest
American Society of Hospital Pharmacists
The People's Pharmacy 2
About Your Medicines
THE ESSENTIAL GUIDE TO PRESCRIPTION DRUGS
JAMES W. LONG, M.D.
THIRD EDITION
THE PHYSICIANS' DRUG MANUAL

Patients who try to learn more from their physician or pharmacist about their medicines are more likely to get such information today than they were 20 years ago. Today there are more patients wanting this kind of information, and more information is available, although patients may have to go out of their way to find it.

Even that is changing. In October, the American Medical Association started a program that encourages physicians to give information sheets about certain drugs to patients for whom they prescribe (see "On Narrowing the Patient-Doctor Communications Gap," *FDA Consumer*, May 1982). The American Association of Retired Persons already has been sending out easy-to-understand leaflets with some of the prescriptions it fills through its mail-order pharmacy service for its senior citizen members (see *FDA Consumer* Updates, July-August 1982).

Some pharmacists keep drug information at the counter for customers.

Evidence of the surge in public demand for information on prescription drugs can be found on all sides. Most pharmacists report that more and more people are asking about their prescriptions. A poll of pharmacists by the Roper Organization in 1978 showed that two-thirds believed it's important to provide patients information along with prescriptions. In 1973, only about half thought so.

Why the growing interest by patients?

Several factors apparently are responsible. More drugs than ever are on the market today. Some have great healing power but they are potent and may have pronounced side effects. As the population grows, there are more people taking medication, with many elderly people taking two or more drugs at a time. This can multiply the chances that harmful drug interactions will occur. So patients have come to recognize that it pays to be knowledgeable about medicine.

Newspapers, magazines, television and radio undoubtedly have contributed to the interest. In the early 1960s, prescription drugs became the subject of Congressional hearings. Television brought the Kefauver hearings on prescription drugs into American homes. Many people learned that drugs have both a generic and a brand name. For the first time, many Americans found out what it was they were taking.

The nation's publishing houses have capitalized on the growing public interest in drugs. A wide variety of books about medicines is now available in bookstores and public libraries. Some of these books are described in this article and in the bibliography that follows.

Generally, they are grouped into four basic categories: Category I books contain detailed prescription drug descriptions. Category II books contain such descriptions with other medical information. Category III books have shortened drug descriptions, while Category IV books discuss prescription drugs in a more general way, along with related issues and health topics. Books are identified by numbered category where mentioned in the text and are grouped under these headings in the bibliography. A fifth category, not discussed in detail in the text, includes books on nonprescription drugs.

The editors of Consumer Union's *Consumer Reports* were among the first to come out with a book on drugs. They published *The Medicine Show* (IV), a 383-page paperback, in 1961. In this and successive editions, over 10 million copies have been sold.

The current edition continues to deal with a variety of drugs, such as cold remedies, aspirin and its competitors, and psychotherapeutic drugs, as well as with health problems.

One fact widely publicized by the Kefauver hearings was that the same drug can cost a lot less when sold under a generic name than when sold by brand name. In 1967 that issue became the subject of a book, *The Handbook of Prescription Drugs* (II), by Dr. Richard Burack. It provided price comparisons between generic and brand name drugs.

It was more than a decade before publishers really moved in behind the lead of Consumers Union and Dr. Burack to satisfy consumer interest about prescription drugs. Patients had to turn to the *Physicians' Desk Reference* (I) (or *PDR*), which contains the information that is based on what the Food and Drug Administration requires on prescription drug package inserts. By the late 1970s, despite its medical language, the *PDR* was a hot item at library reference desks and bookstores (see "Look Who's Reading the PDR Now!" *FDA Consumer*, November 1979).

Publishers of popular books began to see the light. In 1979, *The Pill Book* (III), a paperback, promised to inform the reader about many of the drugs listed in the *PDR*.

This book sold for $3.95 versus about $12 for the *PDR* (the bookstore price for the *PDR* has since climbed to $20). *The Pill Book* started almost immediately to give the *PDR* market competition. It has gone through 15 printings (totaling 1.5 million copies) and is selling 25,000 copies a month.

Others have entered the field. The American Medical Association has brought out its own drug reference, *AMA Drug Evaluations* (I). Entries in the AMA drug reference may include indications (uses) of a drug not included in the FDA-approved labeling.

The physicians' association will sell *AMA Drug Evaluations* to anyone who has the price ($70) and it can also be found at many public libraries.

In 1981 the Biomedical Information Corp. started distributing a manual for patients called, curiously enough, *The Physicians' Drug Manual* (II). Information is presented in two-column charts identical to those in an edition designed for physicians. Indications, administration, contraindications and the like are lined off and flagged in heavy type, making it easier to locate wanted information at a glance. The drug charts cover other information—drug overdoses and drug interactions, for example.

BIC, which has been directing *Drug Therapy* magazine to the medical profession for 12 years, plans to bring out a new periodical, *Rx Being Well*, aimed at educating the consumer and furthering preventive medicine.

The U.S. Pharmacopeial Convention is a nongovernment agency that establishes the official standards for drugs in the United States. According to USP's Executive Director, Dr. William M. Heller, his organization spent nearly $4 million on patient education by the end of 1982.

In 1982 the USP brought forth a new summary of drugs, *Advice for the Patient* (I). It constitutes Volume II of what the USP calls its DI, or dispensing information system. Written for the patient (in contrast to Vol. I of the DI system, which is intended for those who prescribe medications), *Advice for the Patient* includes sections on proper use, side effects, and precautions, as well as information that should be considered before a medicine is taken. USP also grants explicit permission to professionals to photocopy entries for patients.

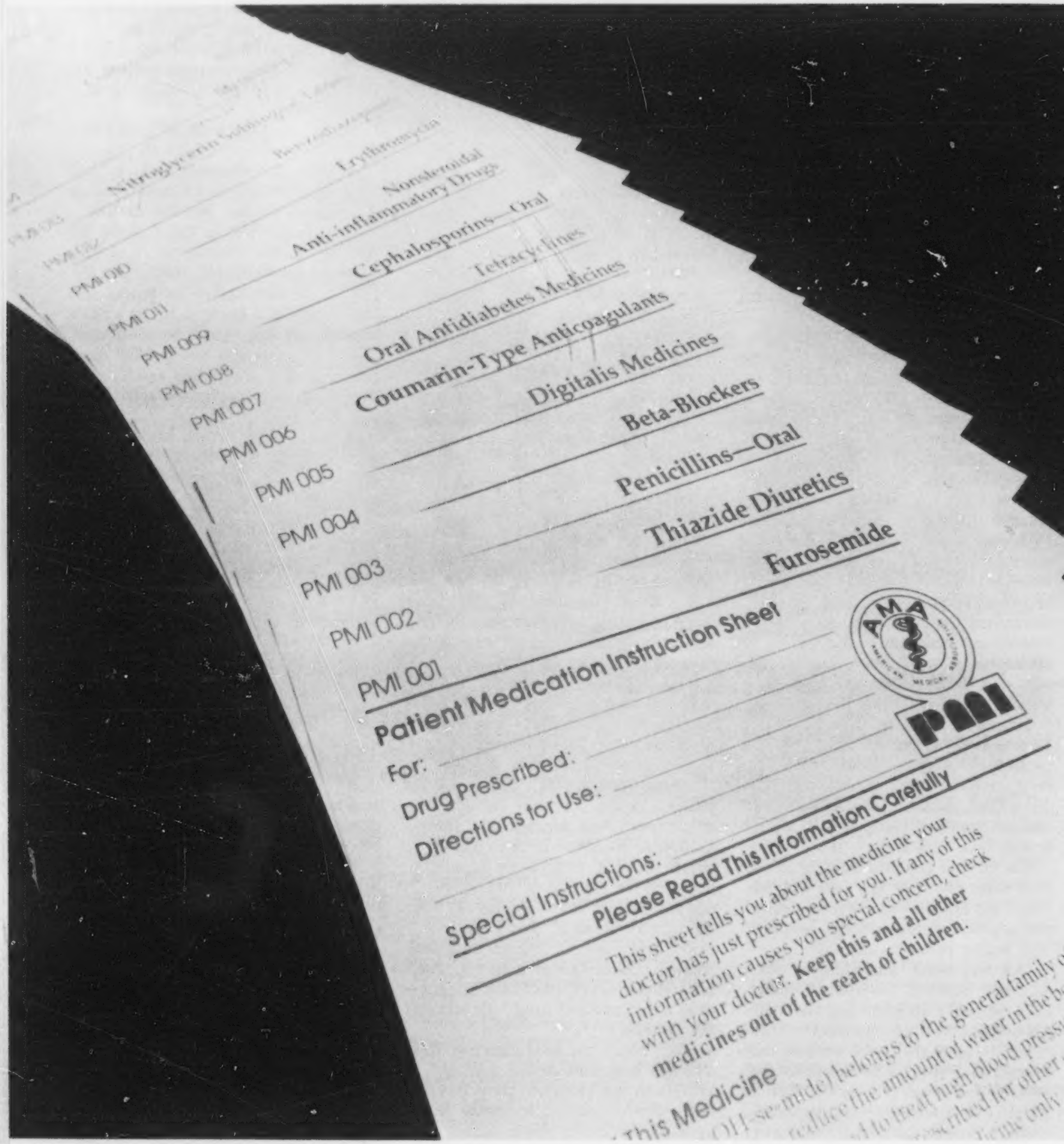
Advice for the Patient can be purchased for $17.95 from USP. An additional $9 will bring bimonthly updates providing information on new drugs.

Dr. James Long's *The Essential Guide to Prescription Drugs* (I) has been in print longer than most. It runs nearly a thousand pages and costs $9.95, a bit more than a penny a page. It describes some 210 drugs in a uniform format covering 23 categories of information. For example, the entry for the drug cimetidine (trade name Tagamet), used to treat duodenal ulcers, is four pages long. Dr. Long tells us how the drug works: "By blocking the action of histamine, this drug effectively inhibits the secretion of stomach acid and thus creates a more favorable climate for the healing of duodenal ulcers."

The Essential Guide is consulted by both physicians and the laity. Among other information, it lays down restrictions on personal habits such as eating, drinking and smoking when taking individual drugs. There is a glossary of medical and technical terms and the book presents comprehensive descriptions of drugs.

Two books published by the USP fall into the same class of pure drug description as Dr. Long's. *The Physicians' and Pharmacists' Guide to Your Medicines* (I) is the more comprehensive and

The AMA's Patient Medication Instruction sheets, which now cover 20 of the most widely prescribed drugs, describe in nontechnical language the purpose of the drug, how it is to be taken, and its possible side effects. PMIs are printed in pads of 100 and can be purchased by physicians for a nominal charge.



Erythromycin
Nonsteroidal Anti-inflammatory Drugs
Cephalosporins—Oral
Tetracyclines
Oral Antidiabetes Medicines
Coumarin-Type Anticoagulants
Digitalis Medicines
Beta-Blockers
Penicillins—Oral
Thiazide Diuretics
Furosemide
PMI 010
PMI 011
PMI 009
PMI 008
PMI 007
PMI 006
PMI 005
PMI 004
PMI 003
PMI 002
PMI 001
AMA
AMERICAN MEDICAL ASSOCIATION
PMI

Patient Medication Instruction Sheet

For:

Drug Prescribed:

Directions for Use:

Special Instructions:

Please Read This Information Carefully

This sheet tells you about the medicine your doctor has just prescribed for you. If any of this information causes you special concern, check with your doctor. **Keep this and all other medicines out of the reach of children.**

This Medicine

boasts over 1,500 entries. Both it and the second book, *About Your Medicine* (I), group entries into drug types such as APC and codeine, appetite suppressants, penicillins, laxatives and the like.

The Consumer Drug Digest (I), which has been compiled by the American Society of Hospital Pharmacists, is written in layman's language and includes entries on more than 200 of the most frequently prescribed prescription drugs, as well as selected nonprescription drugs.

For the most part, the books just described contain detailed drug descriptions only. A second type of popular book of drug summaries seeks to broaden the appeal to consumers by offering additional medical information. Thus, Dr. Judith K. Jones, author of *Good Housekeeping* magazine's *Family Guide to Medications* (II), devotes the first 138 pages to general information about drugs and disease states. Yet the core of the book consists of descriptions of specific drugs.

Books of a third group are quick reference summaries giving essential information about drugs in brief entries. *The Pill Book* (III) falls into this group.

The cover on the *Family Guide to Prescription Drugs* (III) says this slim volume by Dorothy L. Smith contains vital facts about the most frequently prescribed medications. Written in simple, easy-to-understand language, the guide describes the purpose of each drug, its proper use, side effects and special instructions the patient might need.

Edward Stern's *Prescription Drugs and Their Side Effects* (III), 160 pages, is one of the shorter books. Typically, two drugs are described in two columns on each of its pages. Drug precautions, warnings, side effects and adverse reactions predominate in the entries.

Consumer Union's *The Medicine Show* (IV) falls into a fourth group and is one of several without drug descriptions. Books in this group may be the most interesting to the reader who isn't seeking information about specific medications.

The Prudent Use of Medicines (IV), a Time-Life Book, provides a panorama of information about drugs. Quoting William Osler in its opening lines, it asserts, "The desire to take medicine is, perhaps, the great feature which distinguishes man from the animals." The reader is told that in choosing drugs, the promise of the good effect must be weighed against a drug's potential to do harm—the so-called risk-to-benefit ratio of drug therapy.

Although it may make good sense to take a greater risk in, for instance, treating the dying cancer patient with powerful toxic chemicals in the hope of effecting a cure or remission, it is less reasonable to risk serious toxic effects in treating something like a simple headache. Ogden Tanner, author of the Time-Life book, points out that even some who take aspirin for a headache could be running an unacceptable risk. For example, someone with stomach ulcers risks internal bleeding from irritation that can be caused by the acidic aspirin.

Brief drug descriptions are confined to 11 pages in the back of *The Prudent Use of Medicines*. Besides exploring such controversial medical byroads as homeopathic medicine, this illustrated book contains practical advice: how to self-administer drops and ointments, for instance. It also issues useful, if self-evident, reminders: "Read the label of any medicine carefully before you buy it—make sure you know exactly what it is, what it is meant to do, when and how to take it, what the proper dosage is and the precautions to observe."

There are no standard descriptions of the top 200 prescription drugs in Joe Graedon's book about drugs, *The People's Pharmacy—2* (IV). Graedon grapples with some of the current controversy about legitimate medicines. A few of his health recommendations sometimes go against the grain of conventional medical advice. In 1980, for instance, he was pointing out to his readers that some vitamins seem to protect against certain forms of cancer, a notion that since has gained somewhat more medical currency.

The Harvard Medical School Health Letter Book (IV) is an edited collection of discussions from a health newsletter that reaches over 300,000 subscribers each month. It's a grab bag of surprisingly easy-to-read health information based on recent medical findings. A brief four-page chapter on immunization begins by pointing out: "There is no preventive health practice with more payoff than that of immunization." It goes on to describe vaccines currently in common use and offers a schedule that specifies the ages at which they should be administered to children.

Take Care of Yourself (IV), by Dr. James F. Fries, is a self-help guide that outlines a standardized diagram of steps to follow as the symptoms of an illness progress, and tells when to call in a doctor.

Books of this type provide general information that helps in understanding specific drugs and aspects of current medical practice. So armed, the knowledgeable patient is more able to ask a pharmacist or doctor the right questions.

If the public buys and uses books such as these the results should be positive, for patients better informed about the drugs prescribed for them are more likely to understand and comply with instructions for taking them.

Less tangible benefits also are becoming apparent. The better informed patient is apt to assume more responsibility for his or her medical treatment. The physician-patient relationship is coming to be regarded as a collaborative one in which the patient's contribution should be a factor in prescribing.

FDA currently is completing a survey to determine where consumers are getting information about drugs: from doctors, pharmacists or other sources such as radio and television, magazine articles or books. Based on responses from some 1,500 randomly selected consumers, the survey will provide a baseline for measuring progress in patient education. About a year and a half from now, a second survey will be made to determine the effect of new patient education efforts such as that of the AMA.

Egon Weck is a freelance writer.

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Category II—Rx Drug Descriptions with Other Medical Information

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The Pill Book, Harold M. Silverman, Pharm.D., and Gilbert I. Simon, D.Sc. Bantam Books, New York, N.Y., 1979. 418pp, $3.95.

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Category V—Information on Nonprescription (OTC) Drugs

Handbook of Nonprescription Drugs (Seventh Edition), American Pharmaceutical Association, 1982. 682pp, $40.

Physicians' Desk Reference for Nonprescription Drugs, Medical Economics Co. Inc., Oradell, N.J., 1982. 341pp, $12.25.

The Notebook

The Notebook: a potpourri of items gathered from FDA news releases, the Federal Register *and other sources. The* Federal Register *(designated* FR*, with date of publication) is available in many large public libraries.*

■ FDA's pilot program to require pharmacists to distribute **patient information leaflets** with 10 common drugs was rescinded effective Sept. 7, and the 37-year-old batch certification program for **antibiotics** ended officially Oct. 1 (*FR* Sept. 7).

■ The Health Care Financing Administration of the Department of Health and Human Services has ruled that after Sept. 22, 1982, **DMSO** will be covered only when administered for the treatment of interstitial cystitis (*FR* Sept. 22).

■ The Drug Enforcement Administration has proposed rescheduling the narcotic drug **buphrenorphine** from Schedule II to Schedule V, the strictest section of the Controlled Substances Act (*FR* Sept. 20).

■ **Three color additives** have been granted permanent listing effective Oct. 29: FD&C Blue No. 1 for use in externally applied drugs and for general use in cosmetics, except in the area of the eye, and D&C Red No. 27 and D&C Red No. 28 for general use in drugs and cosmetics (*FR* Sept. 28).

■ GRAS LIST: FDA has proposed that the following **gases** be affirmed as generally recognized as safe (GRAS) for direct human food ingredients: carbon dioxide, nitrogen, helium, propane, iso-butane, n-butane and nitrous oxide. Helium is used as a processing aid, and the others serve as propellants and aerating agents (*FR* Oct. 1) . . . . Also proposed for GRAS consideration are **riboflavin** and riboflavin-5'-phosphate, used as a nutrient supplement (*FR* Sept. 14), and **benzoyl peroxide**, a bleaching agent in food, and the flavoring agent **tannic acid** (*FR* Oct. 1).

■ FOOD STANDARDS: FDA is proposing to remove the standards of identity for canned **apricots, cherries, peaches or pears with rum** since no manufacturer is producing these foods (*FR* Sept. 21). . . . The agency is no longer considering the establishment of a U.S. standard for **fructose** and for **virgin olive oil**, refined olive oil, and refined olive residue oil, based on the Recommended International Standards, because there is no interest in or need for such a standard (*FR* Sept. 21 and 24).

■ The new name of the recently combined FDA Bureau of Medical Devices and Bureau of Radiological Health is the **National Center for Devices and Radiological Health**. . . . **Dr. John Petricciani** has been named director of FDA's Office of Biologics. He formerly was assistant director for clinical research in the Bureau of Biologics.

Correction: A Notebook item in the September issue of *FDA Consumer* incorrectly advised readers that the snake venom product PROven could be obtained by Florida residents on a limited experimental basis, under a license granted by the Florida Department of Health and Rehabilitative Services. On March 30, 1982, U.S. District Judge Joe Eaton issued an Order of Permanent Injunction prohibiting the manufacture and distribution of PROven unless and until certain provisions (including current Good Manufacturing Practices, label misbranding, FDA licensing, and others) are met. Until these provisions are met, the Miami Serpentarium is prohibited from manufacturing or distributing PROven in Florida or any other state, or from exporting PROven. The Florida Department of Health and Rehabilitative Services issued the Miami Serpentarium Laboratories Inc. a permit limited to all existing court orders issued by the U.S. District Court. The letter from the state further declared that "nothing in the letter shall be construed to permit any activity or conduct which is violative of any federal law or regulation."

Investigators' Reports

All Right, Santa, Where's The Red Dye No. 2?

by E. Pitt Smith

Once upon a time, about early September, FDA's Buffalo District office received a telephone complaint from an irate consumer. A woman had found some odd-looking animal hair imbedded in a peppermint candy cane her child had been eating. The little girl had become mildly sick to her stomach, and the woman wanted to know what FDA was going to do about filth in candy canes.

A Buffalo District investigator was able to obtain the half-eaten candy cane plus additional samples of candy canes still wrapped in sealed cellophane. According to the mother, the candy had been in the house since the previous Christmas and had turned up only as a result of her cleaning out her pantry. The woman could not remember where she had obtained the candy, but finally recalled it had appeared in the child's Christmas stocking hung on the mantel the night before Christmas.

Analysis of the samples at the Buffalo District laboratory revealed that all the candy canes contained small quantities of reindeer hair.

Color analysis was also performed and revealed the presence of the dye FD&C Red No. 2, which was banned by FDA in 1976. As with all consumer complaints, FDA headquarters was informed of the situation. It was concluded the candy could have originated only with Santa Claus. Inspection of Santa's Workshop was ordered because of the possibility of insanitary conditions and use of a banned dye in a food product.

Buffalo District was asked to undertake the inspection because: 1) the Anchorage, Alaska, Resident Post, FDA's northernmost office, was inundated with other work; 2) Buffalo District investigators were used to extreme cold and a hostile climate; and 3) the Buffalo District staff still believed in Santa Claus.

The following day, after being briefed on international inspections and political acuity (by the District Director's Policy Advisory Committee), the investigator began his journey. Because of Santa Claus' international status, the Canadian Health Protection Branch agreed to assist FDA. Consequently, the investigator proceeded directly to Ellesmere Island in Canada's Northwest Territories and took off in a ski plane furnished by the Canadian government. The pilot headed toward the North Pole. Soon the investigator saw a small island in the Arctic Ocean containing a large factory, a flag, a mailbox, and numerous stables and stock pens where reindeer milled about and munched lichens and frozen alfalfa hay. The pilot unloaded the investigator and his equipment on the frozen ground, and promised to return in three days.

The investigator was not able to begin the inspection until the following day because Santa was away for the day on a trip and no one had been left officially in charge at the plant. After a night spent in the stable with the reindeer, the investigator was able to issue a Notice of Inspection to Santa, who was cooperative and showed him around the plant. Santa stated no complaints had ever been made against him prior to this time.

In the raw material storage area the investigator immediately spotted hundreds of five-gallon buckets labeled "FD&C Red No. 2." Santa explained that large quantities of this coloring agent had been purchased by the elves "at rock-bottom prices" back in 1976. Examination of the storage area for bagged sugar, flour and other dry products revealed small excreta pellets everywhere and creatures that appeared to be lemmings scurrying into corners. The investigator began collecting samples to document the contamination as well as samples of the red dye.

The investigator returned to the plant early the next morning before operations began. In the mixing rooms, storage areas and packaging areas he saw hundreds of Santa's elves brushing and cleaning their reindeer and trimming and polishing hooves for the upcoming Christmas season. In the large open storage area, 10 elves were mounted on reindeer, playing polo. Obviously, this was the source of the reindeer hairs in the candy.

Although the investigator had been instructed to concentrate his attention on food production problems, he obtained a complete product listing from Santa for FDA's files. The factory mainly produced toys that came under the Consumer Product Safety Commission's jurisdiction, but a few toys contained items regulated by FDA: candy pills in kiddie doctor kits; ingredients in cake baking sets that came with little toy ovens; kiddie cosmetics containing FDA-regulated colors. Close to the end of the second day, the investigator wandered into the adult Christmas gift area and saw Santa's elves preparing candies filled with scotch, cognac, cordials and other kinds of alcohol. Since these are banned under the U.S. Food, Drug, and Cosmetic Act, the investigator made a note to mention them to Santa.

After another night in the reindeer stable, the investigator met with Santa to discuss the objectionable conditions

he had discovered during his inspection. Santa agreed to make corrections, beginning with disposing of the Red No. 2. This was poured out on the ground in an outlying area, and emergency orders were sent for replacement colors. An intensive clean-up operation had already been launched by Santa where the lemming population had been seen in the storage area: Lemming holes and other means of entry to the area were closed and repaired, and the little animals were being caught and removed.

Santa produced a plant directive published months earlier forbidding the presence of reindeer in the plant and he promised to reinforce the order with the elves. He showed the investigator a memo, written only the night before, threatening to cancel Christmas if his directives were not obeyed. Such a cancellation, of course, would result in something like 100 percent unemployment among the elves.

As for the liquor-filled candies, Santa flatly refused to dispose of this product. He reminded the investigator that these delicacies are appreciated worldwide and that the United States is the only nation out of step in this matter.

He pointed out, also, that the United States was the only country ever to send anyone to inspect him at the North Pole. If FDA persisted, Santa hinted, all the agency's employees might wake up on Christmas morning and find reindeer droppings in their stockings instead of candy canes.

Santa promised complete and lasting correction of the problems in his factory, and then it was time for the Canadian pilot to return with the ski plane. The investigator didn't know it then, but it would be his only visit to the North Pole. Santa's factory was never located again despite every effort to find it. As the aircraft took off and the investigator looked out the window and watched the reindeer pens growing smaller and smaller, he thought, "If I find that in my stocking on Christmas morning, I'll just use it in my garden next spring."

E. Pitt Smith is director of FDA's Buffalo District.

Mystery Molé

A complicated story involving a truck that was not stolen and a trailer with a hidden compartment was unraveled by FDA investigators in Dallas in the early months of 1982.

It began when U.S. Customs agents at Laredo, Texas, searched a tractor trailer coming over the border from Mexico. Concealed in a false front of the trailer were 415 cases of molé, a highly spiced sauce made with chocolate, chilies and other ingredients that is popular with Hispanics in the Southwest.

This particular brand of molé, Donna Maria, is not allowed entry into the United States because it consistently has been found contaminated with insects and rodent filth.

Ownership of the truck was traced to Jose de J. Esqueda, who operates a retail food store in Dallas. He admitted that the truck was his, but said it had been stolen. He also said he did not know the truck driver.

Wondering about this sizable shipment of a banned food product, investigators from FDA's **Dallas District** and the **Texas Department of Health** checked local stores catering to Hispanic communities. They found quantities of molé supplied by Esqueda and two other wholesalers, and seized several lots of the product. With this information, they met again with Esqueda, who said he knew nothing about Donna Maria molé and had no food storage facilities.

But the investigators had a warehouse address—5800 Maple Avenue in Dallas—that Esqueda remembered as being his. There the investigators found adulterated molé and other food products, which were seized under court order. Earlier, a retail store employee had identified the truck driver in Laredo as having worked for Esqueda.

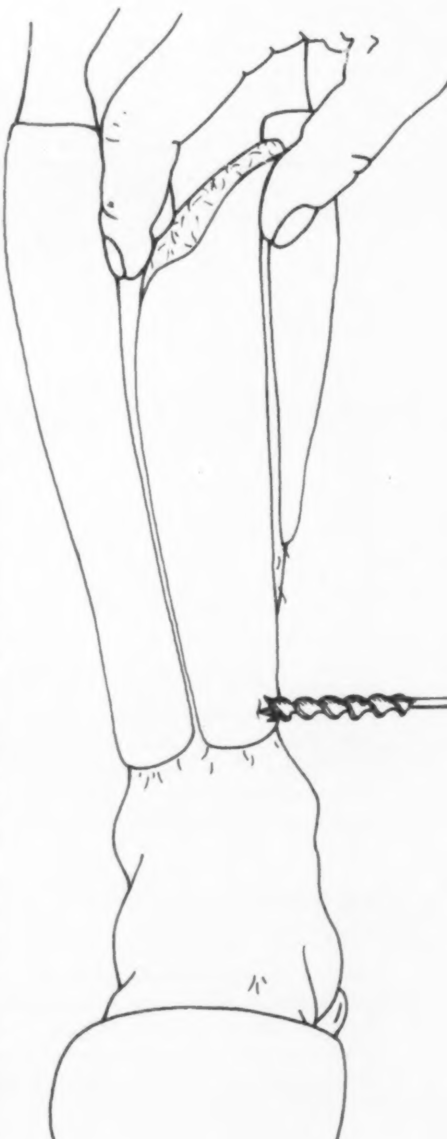
In the course of the investigation, Texas authorities had embargoed products at the warehouse. A few weeks later they found that some of these had been removed. For his role in that, Esqueda was fined by a state court. He also took a $35,000 loss on products ordered destroyed by the federal court, and lost the truck and false-fronted trailer, which were seized and kept by Customs agents.

Buried Flour

A trucking firm in Kansas City made the mistake of placing a load of flour close to a shipment of paint thinner for a long shared ride to Denver this past summer. When the trailer arrived at its destination terminal, the manager and dock supervisor noticed a strong odor of paint thinner, and guessed that the flour might have been contaminated by the thinner. They set aside the flour, and sent the thinner on to its consignee. Then a **Colorado Department of Health** sanitarian took samples of the flour and a saved sample of the paint thinner to the health department laboratory. There an analysis confirmed the contamination. The trucking firm agreed that the flour was contaminated and the entire load, some 6,000 pounds valued at $1,500, was buried in a local landfill.

Leggo!

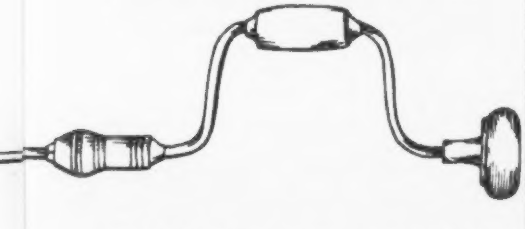
A hair removal wax created more problems than it solved for some consumers. After being allowed to cool and harden on the skin, the wax refused to budge when customers tried to peel it off. The problem was that they hadn't followed directions, but that didn't stop 77 from complaining to the manufacturer and two from taking their problems to FDA.



Last spring, consumers in Boston and

San Francisco notified their local FDA offices that an epilatory product, "Gently Bare Wax Hair Removal System," manufactured by the Andrea Raab Corp. of Brooklyn, would not come off after application to the skin. In contrast to a depilatory, a chemical compound that works by softening the hair into a mass that can be wiped off, an epilatory product consists of wax that is spread on the skin and when removed pulls the hair out of the follicles.

Investigators from FDA's **Brooklyn District** visited the firm in May to follow up the complaints. Examination of the firm's files revealed 77 complaints received between mid-March and May. Some consumers suffered raw, irritated skin or rashes and blotches after having trouble in removing the product from their skin. Most complaints were about irritation on the legs, but some reported irritation of the facial and pubic areas.



Some victims reported using turpentine, gasoline, paint or nail polish remover, kitchen knives, lighter fluid and household cleaners in attempts to remove the wax. One consumer visited a hospital emergency room for aid, two went to pharmacists (who referred them to physicians), and another consulted a dermatologist.

The firm claimed the problem arose because consumers failed to follow directions on the label. Epilatory users normally wait for the wax to harden before it is removed from the skin, but the "Gently Bare" instructions told consumers to remove the wax *before* it hardened. Many apparently failed to read or heed this advice.

The firm decided to recall the product and consider reintroducing it with revised directions for use. FDA determined that the product posed a limited, acute dermal hazard and designated the recall as Class II. This covers temporary or medically reversible effects, with serious injury unlikely. By early fall 1982 nearly 38,000 packages had been recalled.

Slow To Go

Two years ago, FDA's **Kansas City District** obtained a court order for seizure of the contents of a warehouse owned by Chemvet Laboratories, a veterinary manufacturing and supply firm in Olathe, Kan. The firm had a long history of problems with its products and manufacturing methods, and had made the decision to go out of business.

That was fine enough for Chemvet, but it left behind liquids for injection and for topical applications, powders, ointments and tablets, chemical reagents and various drug components, all in assorted containers, labeled and unlabeled.

Many of the products had been recalled because of flaws and defects, and the firm had assured FDA that all materials would be safely disposed of when the manufacturing operations shut down.

But they were not. Instead they were moved from the plant to a warehouse, which is where FDA found them when the court-ordered seizure was carried out.

The seized goods were forfeited in early 1981, since there was no company to claim them. The court ordered that they be destroyed "in a manner consistent with state and federal environmental laws."

This was easier said than done. The U.S. marshal who had custody of the warehouse contents decided his office had neither the resources nor expertise to carry out the court's instructions. He asked the court to transfer the responsibility to FDA. The marshal had, however, taken the tons of drugs and chemicals from the warehouse and stored them in two huge cargo trailers.

A partial inventory was made and referred to the Environmental Protection Agency to determine which materials were hazardous and required special handling and disposal, and which were nonhazardous and could be buried in a landfill. This review took several months.

By October 1981, some 35,000 pounds of the condemned goods had been identified as nonhazardous and were trucked to a local landfill. But a great many items were found in the trailers that had not been on the inventory. This required more time and evaluation, with the Kansas Department of Health finally deciding that most of the remaining materials could be ruled nonhazardous and be buried.

The College of Arts and Sciences at Kansas State University at Topeka had agreed to accept all hazardous drugs, chemicals and other materials if they could also acquire some nonhazardous materials for classroom use. Under this arrangement, the university received some 150 different chemicals and compounds, totaling almost 6,000 pounds.

When all these transactions had been completed, there still remained 25,000 pounds of nonhazardous chemicals and veterinary products. FDA had these hauled to a landfill and buried in June 1982, almost two years after Chemvet went defunct and left FDA, EPA and the courts to pick up the pieces.

—This small sample of reports from the field was compiled and written by Annabel Hecht, Louise Fenner and Richard Thompson.

Notices of Judgment

NOTICES OF JUDGMENT on Seizure Actions

FOOD/Contamination, Spoilage, Insanitary Handling

Cauliflower, frozen, and **other frozen food stocks,** at Norfolk, E. Dist. Va.
Charged on or about 4-30-79: when shipped from Harrington, Del., the articles had been held under insanitary conditions due to a warehouse fire; 402(a)(4). The articles were claimed by Landsman Packing Co., Red Hook, N.Y., and the action was transferred to the District of Delaware, where a consent decree authorized release for reconditioning. (F.D.C. No. 62276; S. No. 79-150-646; N.J. No. 1)

Corn, frozen, and **other frozen food stocks,** at Philadelphia, E. Dist. Pa.
Charged 5-3-79: when shipped from Harrington, Del., the articles had been held under insanitary conditions due to a warehouse fire; 402(a)(4). The articles were claimed by Landsman Packing Co., Red Hook, N.Y., and the action was transferred to the District of Delaware, where a consent decree authorized release for reconditioning. (F.D.C. No. 62274; S. No. 79-156-545; N.J. No. 2)

Eclairs, frozen, frozen fish, frozen juices, and **other frozen foods,** at Harrington, Dist. Del.
Charged 3-8-79: while held by Burris Warehouse Co., Harrington, Del., some of the articles were unfit for food due to the odor of smoke, and all of the articles had been held under insanitary conditions, due to a warehouse fire; 402(a)(3), 402(a)(4). The articles were claimed by Landsman Packing Co., Red Hook, N.Y., and others.

The U.S. marshal had appointed an employee of the named claimant as custodian of the foods. An initial consent decree of condemnation authorizing release to that claimant for salvaging was entered. Various lots of the foods were removed from the fire-damaged warehouse and placed in different warehouses in Pennsylvania, Maryland, New York and elsewhere. However, an accurate accounting of the products and their location was not rendered to the government, and access for inspection by FDA agents was impeded. Accordingly, the government moved for an accounting by the claimant and his agents. Landsman Packing Co., claimant, for itself and others, provided an "approximate" count of the foods and their location in nine different warehouses.

Meanwhile, the government put into effect various re-seizures of the foods at the various locations outside the state of Delaware. Subsequently, a stipulation of consolidation was entered into, together with a consent decree of condemnation in which the parties agreed that the original consent decree of condemnation ought to be treated as dispositive of all claims. Mordan Corp. also intervened in the action, the parties served written interrogatories and litigated their interests, and the government moved for forfeiture of the bond of Landsman Packing Co. The court issued a memorandum opinion saying:

"The United States initiated this forfeiture proceeding under the Food, Drug, and Cosmetic Act (21 U.S.C. §334), alleging that various articles of food had been adulterated within the meaning of the Act as a result of a fire in the warehouse in which they were stored. Landsman Packing Company ('Landsman') filed a claim, and entered into a Consent Decree of Condemnation on April 27, 1979.

"Landsman undertook posting a penal bond of $500,000 to assure its compliance with the substantive provisions of the decree. These required Landsman, *inter alia*, to obtain the FDA's authorization before attempting to reprocess any of the adulterated goods; to permit the FDA to make appropriate examination and inspections; and to compensate the United States for the costs of reasonable supervision and inspection. (Doc. No. 16). The United States, alleging that
Landsman has twice violated the terms of the decree, now se
complete forfeiture of the bond.

I

"The first matter presented for decision is the government's
for a protective order limiting Landsman's examination of seve
employees whose depositions it has noticed. The United States
to bar inquiry into the following areas:

"1. The reasons why the United States decided to seek forfei
the claimant's bond instead of another remedy which was
available to the United States;

"2. The contents or review of any and all memoranda wri
government counsel;

"3. The contents or review of any and all memoranda wri
FDA employees seeking advice of government counsel and/or
information to counsel and/or giving information to counsel
counsel had requested in connection with preparation for litiga
the instant case;

"4. Any and all information directly pertaining to any p
criminal investigation by the FDA of the claimant or its agen

"5. Discovery of any and all remedial actions recommended
FDA against other persons who have violated Court decrees
in other cases brought under the Federal Food, Drug, and Co
Act.

"The government seeks this protection because it believes t
information sought in these areas is both irrelevant and priv

"The attorney-client privilege plainly comprehends the m
described in paragraph 3 so long as these communications wer
in confidence. Likewise memoranda written by government
are protected by the attorney-client privilege if they 'encom
reflect the thoughts and confidences of the client.' *Coastal C*
Duncan, supra, 86 F.R.D. note 3 at 520; *see also United S*
Amerada Hess Corp., 619 F.2d 980 (3d Cir. 1980); *Hercules,*
Exxon Corp., supra, 434 F. Supp. at 144. Finally, those mem
which reflect the attorney's own thought processes in prepara
litigation are protected from discovery by the work product pr
NLRB v. *Sears, Roebuck & Co.*, 421 U.S. 132, 154 (1975).

"Claimant's brief addresses only the relevance issue. It argu
there are terms used in the consent decree which are ambiguo
that it is entitled to discovery within the scope of the govern
five items in order to secure evidence which will be helpful in c
ing those terms. I find this theory unconvincing. The decree spe
itself, and, in any event, the evidence which claimant seeks to d
will not help to elucidate its terms. The disputed discovery is
not designed to aid in determining the meaning of the agreem
tween the parties.

"Judge Latchum confronted a very similar discovery req
United States v. *Readers Digest Association*, 25 F.R.S.2d 1
Del. 1978). Claiming that the terms 'simulated check' an
fusingly simulated items of value' in an FTC consent orde
vague and subjective, Readers Digest sought to determi
whether the FTC staff applied any objective criteria in d
whether advertising materials violated its consent order; (2
interpretations of the clause of the consent order in question we
by the FTC and/or its staff; and (3) why and how the FTC dec
seek civil penalties in this particular case.' *Id.* at 1304. To acco
that purpose Readers Digest deposed two FTC attorneys invo
the compliance proceedings. It later sought to compel further a
from the deponents. The Court concluded: 'The usefulness of s
inquiry generally is doubtful, . . . it is the court which must

whether the advertising materials at issue were covered by the order. The Court will make that decision based on the language of the order, the complaint which gave rise to it, and, to the extent they may be relevant, any communications between the staff of the FTC and Readers Digest. Why or how the FTC decided to institute this civil penalty action is absolutely irrelevant.' *Id.* at 1305.

"Given the tenuousness of the claimant's articulated theory of relevance, one suspects that the motivation of questioning within the scope of Items 1 and 5 is to seek evidence supporting its claim of 'discriminatory enforcement.' Assuming for the present that such a defense, on some set of facts, would be legally viable, it is clear that intrusion into the deliberative process of government is not permitted absent some threshold showing of impropriety. . . . No such showing has been made here.

"It follows that most if not all of the discovery which would fall within the government's five items would be inappropriate. It does not follow, however, that a protective order should be entered. If the claimant, after considering the views herein expressed, wishes to go forward with the depositions, it should do so. In response to specific questions, the FTC may state its position and an ultimate determination may be made in a less abstract context.

II

"The second issue presented to the Court is the motion to dismiss a counterclaim against Mordan Corporation, the intervening claimant, by Landsman for breach of contract. Mordan intervened in this action to obtain a declaratory judgment asserting its right to conduct a warehouseman's sale of goods which a Landsman subsidiary stored in its warehouse pursuant to the condemnation decree. Spring Valley allegedly ceased to pay rent owing to Mordan in October 1980. Mordan asserted an interest in the *res* of the condemnation proceeding pursuant to §§7-209 and 7-210 of the Uniform Commercial Code as enacted by the State of New York, which was represented by neither party to the forfeiture action.

"Subsequently, Landsman filed a counterclaim contending that Mordan had breached its lease agreement with Spring Valley, a New York corporation and a Landsman subsidiary, by failing to maintain temperatures proper for the storage of the goods. Such a claim is proper under Section 7-210, and may be litigated between the parties in the courts of the State of New York. I must decide whether jurisdiction also lies in this Court.

"Landsman's counterclaim contains no express statement of jurisdiction, which alone would warrant dismissal under Rule 8(a)(1), F.R.C.P., unless it is a compulsory counterclaim under Rule 13(a), F.R.C.P. . . . Landsman asserts that its 'claim is clearly compulsory under Rule 13. It arises,' so it is said, 'from the transaction which forms the subject matter of Mordan's claim for declaratory relief—Mordan's storage of the goods.' (Doc. No. 82 at 9) This argument misconceives the 'logical relationship' test which governs this Court's ancillary jurisdiction over compulsory counterclaims. Although Mordan's asserted interest in the *res* subject to the jurisdiction of this Court through the forfeiture action results from its bailment of Landsman's property, the lease agreement itself is not placed in issue. Landsman does not deny that goods which are part of the *res* are in storage in Mordan's warehouse; or that Mordan would not be entitled to a remedy under the UCC if its allegations are true. The only relief which Mordan seeks from this Court is a declaration that it will not violate the April 1979 condemnation decree by pursuing its avenue for relief under the UCC. Neither does Landsman deny that it may protect its rights through Section 7-210 of the UCC.

"As this Court wrote in ***Wolfson* v. *Artisans Savings Bank***, 83 F.R.D. 552, 555 (D. Del. 1979): 'The issues may be related "in a purely transactional level" but the legal and factual claims involved in the two causes of action are virtually unrelated. * * * The inclusion of these . . . counterclaims would only add confusion to an already complex case, without significant benefits to either the Court or the defendants. If the defendants wish to pursue these claims, they are, of course, free to do so in state court.' *See also, Tycom Corp.* v. *Redactron Corp.*, 421 F. Supp. 460, 463 (D. Del. 1976).

"Trial of Landsman's counterclaim necessarily embroils the Court in the resolution of issues completely unrelated to the original forfeiture proceeding, and which are also unrelated to the limited claim for relief asserted in intervenor's complaint. Essentially, Landsman seeks to effect the joinder of a contract dispute with this FDA condemnation proceeding, and to thereby confer jurisdiction on a district court in Delaware, over a transaction arising in New York, between citizens of the State of New York.

"Although Spring Valley, a New York corporation, has assigned its rights under the Mordan lease to its parent, Landsman, it has not thereby created an independent ground of federal jurisdiction. Landsman is, for purposes of diversity jurisdiction, a citizen both of New Jersey, its state of incorporation, and New York, the location of its principal place of business. 28 U.S.C. §1332(c). I need not therefore consider whether Spring Valley's assignment suffices to create diversity which would otherwise not exist. *See Publicker Industries, Inc.* v. *Roman Ceramics Corp.*, 603 F.2d 1065 (3d Cir. 1979), *opinion after remand, Publicker Industries, Inc.* v. *Roman Ceramics Corp.*, Dkt. No. 80-2378, Slip Op. (3d Cir. June 26, 1981). There being no basis for jurisdiction over Landsman's state law counterclaim, it must be dismissed.

CONCLUSION

"The government's motion for a protective order will be denied. Intervenor Mordan Corporation's motion to dismiss Landsman's counterclaim will be granted." (F.D.C. No. 62213; S. No. 79-204-421 et al.; N.J. No. 3)

Flour, beans, and **other food stocks,** at Beckley, W. Va.

Charged 7-14-82: while held by Crook Produce Co., Beckley, W. Va., some of the articles contained rodent and bird filth and all of the articles had been held under insanitary conditions; 402(a)(3), 402(a)(4). Consent decree authorized release to the dealer for salvaging. (F.D.C. No. 63739; S. No. 82-283-865 et al.; N.J. No. 4)

Macaroni products, at Puerto Nuevo, Dist. Puerto Rico.

Charged 5-10-80: while held by Freiria & Co. Inc., Puerto Nuevo, Puerto Rico, the article contained insects and had been held under insanitary conditions; 402(a)(3), 402(a)(4). Default decree ordered destruction. (F.D.C. No. 63714; S. No. 82-275-028; N.J. No. 5)

Peanut butter, at Hereford, N. Dist. Texas.

Charged 7-19-82: when shipped by Portales Valley Mills Inc., Portales, N.M., the articles, labeled in part "Deaf Smith Farms . . . Old Fashioned [or 'Crunchy'] Peanut Butter . . . Distributed by: Deaf Smith Organic Farms, Inc., Hereford, Tex.," and "Arrowhead Mills Deaf Smith Brand . . . Peanut Butter . . . Distributed by Arrowhead Mills, Inc., Hereford, Texas," had been prepared and packed under insanitary conditions—402(a)(4); and some of the articles were in violation of the Fair Packaging and Labeling Act, since the quantity of content statements appearing in the jar labels' principal display panel areas, which were more than five square inches, were in a type size less than ⅛ inch high; and the quantity of contents declaration was not separated from other printed label information appearing above or below the declaration—15 U.S.C. 1453(a)(3)(C)(i), 1453(a)(2). Default decree ordered destruction. (F.D.C. No. 63653; S. No. 82-266-861 et al.; N.J. No. 6)

Peanut butter, crunchy, at Fort Worth, N. Dist. Texas.

Charged 3-8-82: when shipped by Portales Valley Mills Inc., Portales, N.M., the article, labeled in part "Crunchy Peanut Butter . . . Distributed by Generic Products Corp., Fort Worth, Tx," contained insect filth and had been prepared and packed under insanitary conditions; 402(a)(3), 402(a)(4). Default decree ordered destruction. (F.D.C. No. 63652; S. No. 82-266-631; N.J. No. 7)

Walnut cake, frozen, and **other frozen food stocks,** at Elizaville and Milton, N. Dist. N.Y.

Charged 4-30-79: when shipped from Harrington, Del., the articles had been held under insanitary conditions due to a warehouse fire; 402(a)(4). The articles were claimed by Landsman Packing Co., Red Hook, N.Y., and transferred to the District of Delaware, where a consent decree authorized release for reconditioning. (F.D.C. No. 62279; S. No. 79-156-545 et al.; N.J. No. 8)

Walnut cake, frozen, frozen cheese pizza, and **other frozen food stocks,** at Red Hook, S. Dist. N.Y.

Charged 4-25-79: when shipped from Harrington, Del., the articles had been held under insanitary conditions due to a warehouse fire; 402(a)(4). The articles were claimed by Landsman Packing Co., Red Hook, N.Y., and transferred to the District of Delaware, where a consent decree authorized release for reconditioning. (F.D.C. No. 62268; S. No. 79-156-545; N.J. No. 9)

FOOD ADDITIVE

Animal fat, at Delmar, Dist. Del.

Charged on or about 1-23-81: when shipped by Bishop Processing Co., Bishop, Md., the article, labeled in part (shipping documents) "Hydrolized fat - feed grade," contained the nonconforming food additive dieldrin; 402(a)(2)(C). Default decree ordered destruction. (F.D.C. No. 63312; S. No. 81-224-977; N.J. No. 10)

DRUGS/Human Use

Furosemide tablets, thioridazine HCl tablets, sulfamethoxazole & trimethoprim tablets, betamethasone valerate cream, diethylpropion HCl tablets, metronidazole tablets, and **propoxyphene napsylate with acetaminophen tablets,** at Grenada, N. Dist. Miss.

Charged 3-23-81: when shipped by Premo Pharmaceutical Laboratories Inc. (Federal Pharmacal Inc.), South Hackensack, N.J., the articles were new drugs without effective approved New Drug Applications—505(a); and the labeling of the articles lacked adequate directions for use and were not exempted due to their new drug status—502(f)(1).

The articles were claimed by the shipper. Pursuant to stipulation of the parties, the action was transferred to the District of New Jersey for consolidation with similar pending actions. Subsequently, the claimant elected not to pursue the transfer and authorized reconditioning of the articles. Upon joint motion of the claimant and government, the court ordered the articles destroyed. (F.D.C. No. 63420; S. No. 81-275-640 et al.; N.J. No. 11)

Meclizine HCl tablets, at Glasgow, W. Dist. Ky.

Charged 3-19-82: while held for sale, the strength of the article differed from the U.S.P. standard, since the article contained less than 95 percent of the declared meclizine hydrochloride—501(b); and [when shipped by Camall Co., Washington, Mich.] the circumstances of the article's manufacture and processing failed to conform with current good manufacturing practice—501(a)(2)(3). Default decree ordered destruction. (F.D.C. No. 63666; S. No. 82-275-396; N.J. No. 12)

Methaqualone tablets, counterfeit, at West Palm Beach, S. Dist. Fla.

Charged 11-19-81: the article, which resembled a controlled substance drug and which was marked (tablets) "LEMMON 714," was a counterfeit drug which, without authorization, bore the imprint and likeness of a drug manufacturer other than the actual manufacturer and thereby was falsely represented to be the product of such other drug manufacturer; 201(g)(2). Default decree ordered destruction. (F.D.C. No. 63579; S. No. 81-239-727; N.J. No. 13)

Myco Triacet cream, at Niagara Falls, W. Dist. N.Y.

Charged 6-17-82: when shipped by Lemmon Co., South Hackensack, N.J., the article, labeled in part "Myco Triacet Cream . . . Premo Pharmaceutical Laboratories, Inc., South Hackensack, N.J., U.S.A.," had been manufactured, processed, packed and held under circumstances that failed to conform with current good manufacturing practice; 501(a)(2)(B). Default decree ordered destruction. (F.D.C. No. 63728; S. No. 82-312-205; N.J. No. 14)

Sodium, potassium & ammonium bromides solutions, at North Bergen, Dist. N.J.

Charged 9-11-80: when shipped by Murgold Corp., Norwalk, Conn., after manufacture by Ecometics Inc., South Norwalk, Conn., all lots of the article, labeled in part "Serabrina La France . . . contains Sodium Bromide . . . Potassium Bromide . . . Ammonium Bromide . . . Distributed by Murgold Corp., New York, N.Y.," had been manufactured, processed, packed and held under circumstances that failed to conform with current good manufacturin
501(a)(2)(B); the strength stated on lot Q2994 of the ar
from its purported strength, since it contained approxim
cent of its declared bromide content—501(c); lot Q299A
for use as an over-the-counter "Daytime Sedative," was
recognized as safe and effective for its intended use and
ingly, a new drug without an effective approved
Application—505(a). Default decree ordered destructi
No. 63173; S. No. 80-208-390; N.J. No. 15)

MEDICAL DEVICE

X-ray system, Traceray III, at West Frankfort, S. Dist. Ill.

Charged 10-16-79: the article, which had been manu
Western States Supply Ltd., Pueblo, Colo., was danger
when used as directed because it would emit radiation be
set exposure time—502(j); the accompanying labeling w
misleading in claiming compliance with the regulation
and in claiming that the device would deliver the radiati
stated in the instruction manual—502(a); and the article'
below its purported quality—501(c). Consent decree
release to the possessor for reconditioning. (F.D.C. No. 6
79-109-236; N.J. No. 16)

NOTICE OF JUDGMENT on Bond Forfeiture Acti

Landsman Packing Co. Inc., at Harrington, Dist. Del.

Charged 9-18-80 in a motion for forfeiture of a bond and
of a new increased bond: that prior to approval by FDA
ditioning plan, three truckloads of frozen juices had
ditioned upon the orders of the Landsman Packing Co. In
similarly, more than 600 cases of frozen fish products
ditioned without the approval or supervision of FDA.
agreed to a settlement in which $90,000 of the $500,000
ing bond was forfeited and a new bond for $1,500,000
(F.D.C. No. 62213; S. No. 79-204-421 et al.; N.J. No.

NOTICES OF JUDGMENT on Injunction Actions

Leroy Slack, t/a Moreau's Drug Store, Vinton, W. Dist. La.

Charged 6-3-79 in a complaint for injunction: that the de
selling veterinary drugs which were not safe for animal us
der the supervision of a licensed veterinarian (i.e.,
veterinary drugs); that the drugs lacked adequate direct
and were not exempted because the drugs were not sold
order of a licensed veterinarian; that on a number of sp
sions, FDA investigators (without identifying themselves
ployees) selected from a shelf at the defendant's drugs
prescription veterinary drugs which were openly displa
defendant sold the drugs to the investigators without eithe
or receiving a veterinarian's order or prescription; and th
dant had been warned against and was aware of the ille
sale of prescription veterinary drugs without a prescriptio
a veterinarian; 502(f)(1).

A consent decree of permanent injunction enjoined the
of violation and enjoined the open display of prescriptio
drugs on shelves or elsewhere within reach of or accessibl
sons other than the defendant or his employees; and
defendant (prior to selling any prescription veterinary d
complish a number of specified acts including: (a)
procedures so all prescription veterinary drugs will be
area accessible only to employees of the drugstore; (b
prominent sign, readily visible to customers, warning th
tion veterinary drugs might be purchased only by order
tion of a licensed veterinarian; (c) establishing and
records documenting the lawful sale of every prescriptio
drug; and (d) preparing an accurate inventory of all suc
maintaining records and files so as to be able to reconc
with the inventory. (Inj. No. 904; S. No. 79-171-702
No. 18)

Ruth Ashbrook Bakeries Corp. of Seattle, LeConie Stiles Jr., pr

LeConie (Lee) Stiles III, vice president and general manager, Seattle, W. Dist. Wash.

Charged 10-6-80 in a complaint for injunction: that the defendants, at their bakery in Seattle, Wash., manufactured, packed, held and distributed in interstate commerce bakery products made from wheat grown in Washington, Idaho and Montana; that the bakery products had been prepared, packed and held under insanitary conditions; that FDA inspections of the defendants' bakery disclosed a number of specified insanitary conditions and practices; and that there had been numerous warnings to the defendants; 402(a)(4).

A consent decree of permanent injunction enjoined the complained of violations and enjoined bakery operations involving interstate components and interstate shipment of bakery products unless and until: a number of specified methods, facilities and controls for preparing, packing and holding foods were established and operated; a qualified expert certified to FDA that certain requirements had been met; and all food on hand was examined for filth, necessary analyses were made, and all contaminated food was destroyed or otherwise brought into compliance. (Inj. No. 963; S. No. 80-212-495 et al.; N.J. No. 19)

Shetakis Wholesalers of Colorado Inc., and **James L. Shetakis,** president, Denver, Dist. Colo.

Charged 12-11-79 and amended 12-13-79 in a complaint for injunction: that defendants had been engaged in storing and trading various human foods at their warehouse in Denver, Colo.; that food stored in the warehouse was held under insanitary conditions; that some of the food contained insect filth; and that the defendants were well aware that their manner of operation of the food warehouse violated the law; 402(a)(3), 402(a)(4).

A consent decree of permanent injunction enjoined the complained of violations and enjoined placing in the defendants' warehouse, and distributing from the warehouse, any interstate foods unless and until: a number of specified requirements to assure that food was not contaminated were in effect; a qualified expert certified that the defendants had met the specified requirements; and all foods on hand at the defendants' warehouse were examined for filth, necessary analyses were made, and all contaminated foods were destroyed or otherwise brought into compliance. (Inj. No. 931; S. No. 80-198-277; N.J. No. 20)

Tidewater Biologicals Inc., and **F. Eugene Herring,** president, **Lawrence F. Farmer,** vice president, and **Archer D. Farmer Jr.,** secretary-treasurer, Chesapeake, E. Dist. Va.

Charged 7-11-79 in a complaint for injunction: that the defendants, at their Chesapeake, Va., plant, manufactured, processed, packed, labeled and distributed in interstate commerce, *in vitro* diagnostic products, including diagnostic media, reagents and solutions (i.e., products intended for use outside the human body in the diagnosis of disease or in the determination of the state of health in order to cure, mitigate, treat or prevent disease); that the products were held for sale after interstate shipment of their components; that certain such products fell below their purported purity or quality, since they were not sterile; that all of the products had been prepared, packed and/or held under insanitary conditions; that the products had been manufactured, packed and stored under circumstances that failed to conform with the standards applying to the manufacture of *in vitro* diagnostic products; that FDA inspections disclosed a number of specified deviations from current good manufacturing practice; that FDA analyzed a sample lot of the defendants' agar and found air bubbles and visible bacteriological contamination; and that the defendants were well aware that their activities were in violation of the law; 501(c), 501(a)(2)(A), 501(h).

A consent decree of permanent injunction enjoined the complained of violations and enjoined the interstate shipment of any such products from the defendants' plant unless and until: a number of specified conditions concerning good manufacturing practice had been met; the plant had been inspected and certified to meet specified requirements; all such products on hand at the plant and all product components had been examined, necessary tests made, and necessary recalls of finished products were made; and all such examined, tested or recalled products were destroyed or otherwise brought into compliance. (Inj. No. 905; S. No. 79-103-685 et al.; N.J. No. 21)

Notices of Judgment are given pursuant to section 705 of the Federal Food, Drug, and Cosmetic Act. Notices of Judgment report cases involving seizure proceedings, criminal proceedings, and injunction proceedings. Seizure proceedings are civil actions taken against *goods* alleged to be in violation, and criminal and injunction proceedings are against *firms* or *individuals* charged to be responsible for violations. The cases generally involve foods, drugs, devices, or cosmetics which were alleged to be adulterated or misbranded or otherwise violative of the law when introduced into and while in interstate commerce, or while held for sale after shipment in interstate commerce.

Notices of Judgment are prepared by Food and Drug Division, Office of the General Counsel, HHS.

Published by direction of the Secretary of Health and Human Services.

Arthur Hull Hayes Jr., M.D., *Commissioner of Food and Drugs*
Washington, D.C., Dec. 1, 1982

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I certify that the statements made by me above are correct and complete.

Harold C. Hopkins, editorial director, for Roger W. Miller, editor

1982 FDA CONSUMER INDEX

The index of *FDA Consumer* articles for 1982 is in a more detailed format than previous indexes. Specific subjects are listed rather than just the title of articles. This year, for the first time, items in the Updates, Notebook and Investigatiors' Reports sections are included. Subject listings are followed by the volume number, issue number (in parenthesis), and the page or pages on which the subject appears. 1982 issues are all part of volume number 16, which includes this, the December 1982-January 1983 issue. For copies of previous indexes, write to: Editor, *FDA Consumer* (HFI-20), 5600 Fishers Lane, Rockville, Md. 20857.

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